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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 9 1955

THE TREATMENT OF ACUTE LEUKAEMIA*

BY

RONALD BODLEY SCOTT, D.M., F.R.C.P.

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The last decade has seen the focus of haematological interest shift to the problem of acute leukaemia. This disease has been forced upon the clinicians' attention by its steadily mounting frequency; while the research workers have found it a convenient field for the study of chemotherapy in cancer, and as a result of their exertions it has become possible for the first time to influence its course.

The aim of this paper is to review the methods of treatment at present available and to discuss their application and value in the light of experience gained in the past six years.

The Present Series

In this period 121 patients with acute leukaemia have been under treatment. The composition of the series is set out in the Table. The majority of children with this disease are under the care of paediatricians; thus the series must contain a disproportionate number of adults and cannot give an exact indication of the age incidence in the general population.

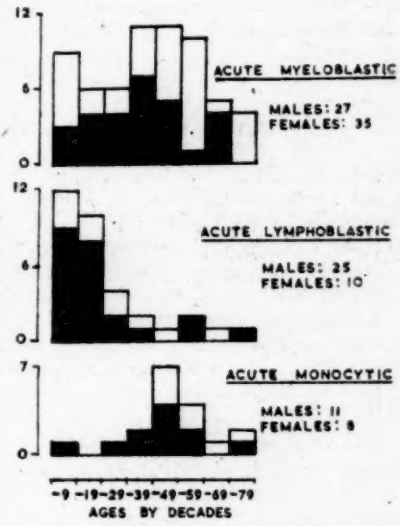
Composition of the Cases of Acute Leukaemia

	Male	Female
Acute myeloblastic leukaemia:		
"Classical" type	26	32
Erythromyelosis	1	3
Acute lymphoblastic leukaemia:		
"Classical" type	12	6
Pure medullary type	7	3
Sternberg type	6	1
Acute monocytic leukaemia	11	8
Acute erythraemia (di Guglielmo)	4	1
Total all types	67	54

The difficulties of cytological classification, and in particular of distinguishing the myeloblast from the lymphoblast, are familiar and inescapable. Nevertheless the figures (see Fig.) show the generally accepted age incidence of the three cytological types of acute leukaemia: myeloblastic, affecting all ages indifferently; lymphoblastic, predominantly children; and monocytic, the middle-aged. Five examples of di Guglielmo's acute erythraemia are included, and four of erythromyelosis are grouped with the myeloblastic leukaemias. Prognosis, in respect of remission, depends largely upon the cytological type of the disease, and classification is thus no longer the sterile academic exercise it once seemed.

*A paper read at a meeting of the physicians of the South-east Metropolitan Region, April 30, 1955.

In this series the patients with lymphoblastic leukaemia have been placed in three clinical categories: the "classical" form, with generalized enlargement of lymph nodes, liver, and spleen in which the blood picture is frankly leukaemic; the pure medullary form, presenting without enlargement of lymph nodes, liver, or spleen, and usually aleukaemic; and the Sternberg (1905) type with local tumour formation, commonly mediastinal, frequently preceding by a few weeks the appearance of leukaemic blood changes. The distinction between the first two varieties is not absolute: all gradations occur, from those with massive splenic and nodal enlargement to those with no trace of either; moreover, with the passage of time these features make their appearance in a proportion of the pure medullary type. Nevertheless there is a practical value in their differentiation, because the patients in whom the proliferative process is at first restricted to the bone marrow have a greater liability to remission than those with extramedullary infiltrations, and, *per contra*, the chances of remission are remote in the Sternberg variety, where the disease is primarily limited to one group of nodes and only later becomes systematized. In this respect the classical form occupies a position intermediate between the two.



Age incidence of acute leukaemia.

The present series illustrates these points. It includes 10 patients, varying in age between 3 and 78 years, with the pure medullary type, and in each some degree of remission was noted. In one it was entirely spontaneous; in five it followed blood transfusion; and in four it was the result of specific treatment. The antithesis is provided by 7 patients, aged 4 to 20 years, with the Sternberg type, in none of whom was any improvement observed.

Treatment

The treatment of acute leukaemia includes measures designed to relieve symptoms resulting from anaemia, infection, and the haemorrhagic state, as well as attempts, which may be termed "specific," to restrain the leukaemic process.

Control of the Leukaemic Process: (1) Blood Transfusion

Spontaneous remissions have been noted in 4 to 10% of children with acute leukaemia (Diamond, 1951; Southam *et al.*, 1951). A review of recorded examples showed that they often followed blood transfusion (Dreyfus, 1948). The use of exsanguination-transfusion derived from this observation, and remissions were reported in 33% of 60 patients so treated (Bessis and Dausset, 1950). The initial inference that a plasma maturation factor was responsible has not been supported by later observations, and it has been suggested that any improvement should be attributed to liberation of cortisone following transfusion shock (Bessis, 1954).

This specific effect of transfusion has been stressed again recently by a report of remissions thus induced in 34% of 41 adults with acute leukaemia (Hayhoe and Whitby, 1955); a much higher figure, it should be noted, than would be expected from the use of cortisone. In the present series 46 patients were treated by blood transfusion alone, and in 9 (19.5%) significant remission followed. Exsanguination-transfusion was undertaken only in three; two died within a few days, and although the third survived for four months the course of the disease did not appear to be altered. The difficulties and dangers of the method have led most workers to discard it.

(2) Antimetabolites

An antimetabolite obstructs the operation of an enzyme system by displacing its related metabolite, and its effects are similar to those resulting from a deficiency of the metabolite itself. The first of these substances to be used in the treatment of acute leukaemia were the folic acid antagonists (Farber *et al.*, 1948), following the observation that the leukaemic process had been accelerated by giving a folic acid conjugate. The biologically active derivative of folic acid, citrovorum factor, is essential for normal haemopoiesis, and some theoretical basis for its deficiency exerting a selective depressant effect upon leukaemic proliferations is afforded by the finding that its concentration in leukaemic cells is five times that in normal leucocytes (Swendseid *et al.*, 1951).

The two folic acid antagonists in common use are aminopterin (4-aminopteroylglutamic acid) and amethopterin (4-amino-N10-methylpteroylglutamic acid). The daily oral dose of the first is 0.5 to 1 mg. for children and up to 3 mg. for adults, and of the second 2.5 to 5 mg. and up to 10 mg. respectively. Treatment may have to continue for as long as eight weeks before remission is procured. Toxic effects may appear within a few days or not for months; the earliest is buccal ulceration, followed by diarrhoea, vomiting, and sometimes gastro-intestinal haemorrhage.

Many reports of the value of the folic acid antagonists have been published. In adults remission is rare, being noted occasionally in lymphoblastic, seldom in myeloblastic, and hardly ever in monocytic leukaemia. In children the results are more hopeful; in an analysis of published series, 68% of 425 cases showed significant improvement (Fountain, 1954). In another report 37% of 119 children responded by complete remission (Burchenal, 1952). In lymphoblastic leukaemia the rate is as high as 60%; in myeloblastic less than 10%. The duration of remission varies from two weeks to two years, the mean lying between two and three months. Second remissions may occur, but thereafter the disease usually becomes resistant to these drugs.

Folic acid antagonists have not been used extensively in the present series: partial remission was obtained in two of three children with myeloblastic leukaemia, and in two of six with lymphoblastic leukaemia. One of two adults with monocytic leukaemia had a short incomplete remission.

The second group of antimetabolites are the purine antagonists, the theoretical rationale being their presumed interference with nucleic acid metabolism. The first shown to have antileukaemic activity was 2:6-diaminopurine (Burchenal *et al.*, 1951), but it was soon supplanted by the more effective 6-mercaptopurine (Burchenal *et al.*, 1953; Fountain, 1955). This drug, given by mouth in a daily dose of 2.5 mg. per kg. body weight, is virtually without toxic side-effects. Treatment is continued for four weeks unless remission occurs sooner. The results are similar to those obtained with folic acid antagonists. In the first report (Burchenal *et al.*, 1953) 15 complete and 10 partial remissions were recorded in treating 43 children, while 4 of 10 adults showed significant improvement. Remission is induced far more readily in lymphoblastic than in the other types of leukaemia. Leukaemia resistant to folic acid antagonists may respond to 6-mercaptopurine. In this series 10 patients have received 6-mercaptopurine:—Myeloblastic leukaemia: 4 adults, no improvements; 1 child, good remission. Lymphoblastic leukaemia: 1 adult, good remission; 2 children, 1 moderate remission. Monocytic leukaemia: 2 adults, no remission.

(3) Steroid Hormones

Cortisone was shown to inhibit the growth of transplanted lymphosarcoma in mice in 1944 (Heilman and Kendall, 1944), but the first reports of its action in human leukaemia were not until 1950 (Pearson *et al.*, 1950; Farber *et al.*, 1950), when satisfactory remissions were claimed in 80 of 175 children and in 14 of 60 adults. An analysis of published series shows that of 425 cases treated with cortisone or corticotrophin (A.C.T.H.), there was complete remission in 29% and partial in 24% (Fessas *et al.*, 1954). In a small group of 47 cases complete remission was reported in 18 of 22 children and in 3 of 9 adults with lymphoblastic and partial in 2 of 15 patients with myeloblastic leukaemia. Remission occurs more rapidly than with antimetabolites, but is of shorter duration and less complete.

The daily dose of cortisone required in acute leukaemia is 200 to 300 mg. by mouth in adults, and up to 200 mg. in children. Corticotrophin is given by intramuscular injection every six hours, in daily doses of 100 mg. for children, or 200 mg. for adults, or by intravenous infusion in children in quantities of 25 to 40 mg. in 8–12 hours.

In the present series 23 patients have received cortisone or corticotrophin:—Myeloblastic: 6 adults (1 complete, 1 partial remission); 4 children (1 complete, 2 partial remissions). Lymphoblastic: 5 adults (3 complete remissions); 5 children (2 complete, 1 partial remission). Monocytic: 3 adults (no remissions).

Symptomatic Treatment

Relief of Anaemia.—The cause of anaemia in acute leukaemia is obscure: haemorrhage must contribute its share; evidence of exaggerated blood destruction is lacking; and defective formation is usually accepted as its basis, although recent studies with radioiron do not support this view (Schapira *et al.*, 1954). Whatever the cause of the anaemia, blood transfusion is the only effective means of relief. Its place in treatment has already been discussed: it may be used in the hope of inducing remission or with the less ambitious aim of maintaining a reasonable haemoglobin level. When an attempt is being made to obtain remission by "specific" treatment, a haemoglobin level of 50 to 60% should be maintained. Transfusion should never be prescribed *faute de mieux*, but should be a purposive measure undertaken in the knowledge that it is impossible to deny a patient repeated tranfusions after he has experienced the benefit that one confers.

Control of Infection.—General and local infections are common in acute leukaemia, and antibiotics should be prescribed in conformity with established general principles. Their prophylactic use is to be deprecated, and it should be noted that fever in this disease does not of necessity indicate a secondary infection. Intramuscular injections in the leukaemic patient commonly cause haemorrhage into

the tissues; thus drugs should, when possible, be given orally. Mouth-washes help to relieve the misery of leukaemic stomatitis. Hydrogen peroxide (1.5%) or a saturated solution of sodium perborate is useful, and citric acid (1 to 1.25%) twice daily for two consecutive days has been recommended (Hayhoe and Whitby, 1955).

Control of the Haemorrhagic State.—Anaemia and infection are both susceptible of treatment, but the liability of the leukaemic patient to bleed still defies control. This tendency bears a general, but not a precise, relation to the level of the platelet count; other factors have been suspected, but have hitherto eluded detection. The importance of the haemorrhagic state is shown by the present series: post-mortem examination was made in 41 cases; in 17 (41%) haemorrhage appeared to be the immediate cause of death, and in 12 (29%) it was intracranial. Platelet transfusion is perhaps the logical method of treatment (Stefanini and Dameshek, 1953), but technical difficulties prevent its general use at present. Recent reports suggest that intravenous injection of a chloroform extract of acetone-washed brain may be of value (Hayhoe and Whitby, 1955). At present, transfusion of fresh blood is the only measure likely to allay the tendency to bleed, and its results are inconstant. Local application of thrombin solution, after careful toilet, is often effective in controlling haemorrhage from the gums.

Prognosis

The outcome of acute leukaemia remains fatal; the only prognostic question to be answered is whether remission will occur. This, it has been shown, is more probable in children under the age of 12 years and in the lymphoblastic variety, particularly of the pure medullary type.

The influence of "specific" treatment on the mean length of survival is difficult to assess. Transfusion and the antibiotics are said to have prolonged the lives of children with the lymphoblastic form from 5.6 to 8.9 months (Bierman *et al.*, 1950). In the present series, of 81 patients treated with blood transfusion and antibiotics the mean length of survival from the first symptoms was 20.2 weeks, and in 34 who also received specific treatment, 20 weeks; in 17 children under 12 years without specific treatment the mean survival was 19.9 weeks, and of 9 with specific treatment 26.8 weeks.

The variable length of survival in acute leukaemia probably deprives these figures of any significance.

Discussion

It is often suggested that considerations of humanity should limit the treatment of acute leukaemia to relief of distress and forbid officious attempts to induce remissions which can never be more than ephemeral. Every physician must answer these questions for himself. It is certain, however, that therapeutic nihilism demoralizes the patient, his relatives, and sometimes the medical attendant; moreover, it ensures that no advance in treatment will ever be made. In this paper it is assumed that efforts to procure remission are desirable.

Management varies with the age of the patient, with the cytological and clinical type of the disease, and with the severity of the illness.

In a child, when high fever and haemorrhagic state indicate rapidly advancing disease, a start should be made with cortisone by mouth or with corticotrophin by intravenous drip. Antimetabolites may be used concurrently, but are better reserved for the first signs of relapse. If the child's condition suggests that he is likely to survive more than three weeks, antimetabolites should be given preference. It is advisable to use 6-mercaptopurine rather than a folic acid antagonist, because its toxic effects are negligible; a change should be made to the second if the disease proves resistant to the first. By employing the various "specific" measures in sequence, changing from one to the next as resistance develops, repeated remissions may be induced in favourable cases. Maintenance treatment, once remission is achieved, has not proved satisfactory, and "specific" drugs are best withheld until the onset of relapse is evident. The first sign of this event is an increase in primitive cells in the bone marrow, but most workers prefer to await changes in the peripheral blood rather than subject children to repeated bone-marrow puncture.

In adults, 6-mercaptopurine should be given a trial if the patient's general condition is satisfactory. It may be combined with or followed by cortisone. The alternative is to watch the effect of blood transfusion alone for a period of two or three weeks; in 15 to 20% of patients it will induce a satisfactory remission. In lymphoblastic and myeloblastic leukaemia cortisone should be given if it becomes apparent that neither blood transfusion nor 6-mercaptopurine is likely to be effective. Monocytic leukaemia is resistant to cortisone, but occasional cases respond to 6-mercaptopurine. The folic acid antagonists have no place in the treatment of acute leukaemia in adults.

Conclusion

The therapeutic position in acute leukaemia has been reviewed. The results of treatment afford no grounds for optimism, but they do show that in some instances and for short spells the leukaemic process can be checked or even reversed. From this observation we must draw hope that a means of controlling this tragic disease will one day be vouchsafed to us.

References

Bessis, M. (1954). In *Ciba Foundation Symposium on Leukaemia Research*, p. 36. Churchill, London.
—— and Dausset, J. (1950). *Rev. Hémat.*, **5**, 188.
Bierman, H. R., Cohen, P., McClelland, J. N., and Shimkin, M. B. (1950). *J. Pediat.*, **37**, 455.
Burchenal, J. H. (1952). *Acta haemat. (Basel)*, **7**, 193.
—— Karnofsky, D. A., Laird Myers, W. P., Escher, G. C., Craver, L. F., Dargeon, H. W., and Rhoads, C. P. (1951). *Cancer*, **4**, 549.
—— Murphy, M. L., Ellison, R. R., Sykes, M. P., Tan, T. C., Leone, L. A., Karnofsky, D. A., Craver, L. F., Dargeon, H. W., and Rhoads, C. P. (1953). *Blood*, **8**, 965.
Diamond, L. K. (1951). Cited by S. Farber, *Proc. Inst. Med. Chicago*, 1951, **18**, 311.
Dreyfus, B. (1948). *Rev. Hémat.*, **3**, 29.
Farber, S., Diamond, L. K., Mercer, R. D., Sylvester, R. F., jun., and Wolff, J. A. (1948). *New Engl. J. Med.*, **238** 787.
—— Downing, V., Kennedy, B. H., Shwachman, H., and Toch, R. (1950). *Blood*, **5**, 787.
Fessas, P., Wintrobe, M. M., Thompson, R. B., and Cartwright, G. E. (1954). *Arch. intern. Med.*, **94**, 384.
Fountain, J. R. (1954). *Edinb. med. J.*, **61**, 69.
—— (1955). *British Medical Journal*, **1**, 1119.
Hayhoe, F. G. J., and Whitby, L. (1955). *Brit. J. Haemat.*, **1**, 1.
Heilman, F. R., and Kendall, E. C. (1944). *Endocrinology*, **34**, 416.
Pearson, O. H., Eliel, L. P., and Talbot, T. R., jun. (1950). *Bull. N.Y. Acad. Med.*, **26**, 235.
Schapira, G., Tubiana, M., Dreyfus, J. C., Kruh, J., Boiron, M., and Bernard, J. (1954). *Rev. Hémat.*, **9**, 3.
Southam, C. M., Craver, L. F., Dargeon, H. W., and Burchenal, J. H. (1951). *Cancer*, **4**, 39.
Stefanini, M., and Dameshek, W. (1953). *New Engl. J. Med.*, **248**, 797.
Sternberg, C. (1905). *Beitr. path. Anat.*, **36**, 437.
Swendseid, M. E., Bethell, F. H., and Bird, O. D. (1951). *Cancer Res.*, **11**, 864.

The Professional Classes Aid Council, of which Lord Moran is president, began the financial year on April 1, 1954, with a deficit of about £1,000, but ended it on March 31, 1955, with a surplus of £1,115, states the council's 34th annual report. This achievement was made possible by a £944 increase in donations and subscriptions; a £583 increase in dividends from invested legacies; and by the £1,656 17s. 3d. response to Lord Moran's wireless appeal. As the B.B.C. will not consider application for a further broadcast for three years, this last sum was divided between the budgets for the current and two succeeding years. In spite of restricted expenditure, 266 families were helped; 76 were new cases. The total number of applications was 471. Of the 205 refused, the great majority were helped to find alternative sources of relief, often from the relevant professional funds. Yearly grants were made to 69 people who, through age or ill-health, will never be self-supporting again; temporary help, often a single gift, was given to the total of £1,531 10s. 1d.; and education grants were made to 110 children and 42 students.

RETROLENTAL FIBROPLASIA IN THE UNITED KINGDOM

A REPORT TO THE MEDICAL RESEARCH COUNCIL BY THEIR CONFERENCE ON RETROLENTAL FIBROPLASIA*

In October, 1951, when very little was known of the aetiology and incidence of retrolental fibroplasia (a disease of premature babies first described by Terry (1942a, 1942b)), a detailed investigation was set in train by the Medical Research Council. Premature baby units in hospitals spread throughout the United Kingdom were asked to complete a questionary relating to each mother during her pregnancy and to the treatment and development of the baby up to the age of 6 months. Observations were recorded at 17 such units during the period October 1, 1951, to May 31, 1953. Initially, the observations were limited to babies of a birth weight of 3 lb. (1,350 g.) or under, but with increasing knowledge this figure was raised first to 3½ lb. (1,600 g.) and finally to 4 lb. (1,800 g.). To make the investigation comprise *all* babies of 4 lb. or under, during the whole of the period October, 1951, to May, 1953, each nursery had to be visited by the investigator in charge of the research and the required data extracted from the case notes. As a result about half the questionaries were completed concurrently by the staff of the unit looking after the infants, while about half were compiled retrospectively by the investigator. Fortunately, good case notes were available for most babies, and it is not thought that serious error or bias has been introduced in this way.

The Survey

During the 20 months of the inquiry 1,999 babies of 4 lb. (1,800 g.) or under entered the nurseries, and the 1,095 of them who survived for at least two months form the basis of this report.† Of these 1,095 babies, 84 (7.7%) showed evidence of a retinopathy, the criterion being the presence of neovascularization in the fundus, which was found during routine ophthalmoscopy performed at regular intervals on all the children. In 39 of the 84 cases there was a subsequent "regression," or return to normal fundi (apart from some peripheral fibrosis); in 45 (or 4.1% of the total 1,095 babies) there was "blindness," implying one or both eyes permanently affected, with almost certain severe loss of vision. (Throughout the report the term "affected" is used to denote a baby with a retinopathy whether it regressed or not, and "blind" or "blindness" to denote a permanent change.)

Members of Conference: Sir Stewart Duke-Elder (Chairman), Professor F. M. B. Allen, Dr. N. H. Ashton, Professor N. B. Capon together with Dr. F. P. Hudson, Professor W. S. Craig, Dr. Mary Crosse, Dr. R. H. Dobbs, Mr. J. H. Doggart, Professor R. W. B. Ellis, Professor W. F. Gaisford, Professor S. G. Graham together with Dr. R. A. Shanks, Professor A. Bradford Hill, Dr. Katherine Hirst, Professor R. S. Illingworth, Dr. F. J. W. Miller, Professor A. A. Moncrieff, Professor A. V. Neale together with Dr. Beryl Corner, Dr. B. E. Schlesinger, Dr. Victoria Smallpeice, Sir James Spence (until his death in May, 1954), Professor A. G. Watkins together with Dr. J. Jacobs, and Miss Iris Kane (investigator in charge of the research).

This report was prepared by Miss Kane, and the Conference is glad to acknowledge her services throughout this research. The Conference is greatly indebted to Dr. W. J. Martin, of the Medical Research Council's Statistical Research Unit, for assistance in the analysis of the data.

†A few of them (40) were not seen after the age of 6–8 weeks, but these were babies at the top of the weight scale and their eyes were all normal on discharge. Twelve with normal eyes died between the ages of 2 months and 6 months, but are included.

Aetiology

Maternal Factors

Age of Mother.—There were slightly more older women amongst the mothers of affected babies (48.8% aged 30 and above) than amongst those of the unaffected (37.7%), but the difference is not more than might quite easily arise by chance. Many other authors have observed this lack of significance in the mother's age (Gilger, 1949; Unsworth, 1949; Speert *et al.*, 1950; Ryan, 1952).

Syphilis.—Syphilis was present in only one affected and one unaffected baby.

Rhesus Factor.—Four unaffected babies, but no affected, had a rhesus incompatibility which caused symptoms. Other workers also have reported that the development of a retinopathy is not related to rhesus incompatibility (Crosse, 1950; Speert *et al.*, 1950).

Illness During Pregnancy.—In this respect information was available for the mothers of only 64 of the affected babies and 808 of the unaffected (approximately 75% of each group). So far as the information goes, there was no appreciable difference between the two groups. No case of rubella was recorded, but seven other specific fevers were noted amongst the mothers of the unaffected babies (0.9%) and two amongst the mothers of the affected babies (3.1%). The results are in keeping with the observations of other workers (Gilger, 1949; Crosse, 1950; King, 1950).

Cause of Prematurity.—In many cases (41% of the unaffected babies and 30% of the affected, see Table I) the cause of the prematurity was not known. There was no significant difference between the affected and unaffected groups in respect of the incidence of known causes of prematurity—pre-eclampsia, multiple births, ante-partum haemorrhage, and maternal disease. Similar conclusions have been drawn by other authors (Gilger, 1949; Unsworth, 1949; Speert *et al.*, 1950; Kinsey, 1951; Platou, 1951; Lelong *et al.*, 1952).

TABLE I.—*Cause of Prematurity*

Cause of Prematurity	Babies with No Retinopathy		Babies with a Retinopathy	
	No.	%	No.	%
Pre-eclampsia	225*	22·3	19	22·6
Placenta praevia	35	3·5	2	2·4
Ante-partum haemorrhage (of unknown origin)	54	5·3	9	10·7
Maternal disease:				
Heart disease (other than hypertension)	13	4·0	1	8·3
Kidney disease (other than nephritis)	3		2	
Respiratory infection	6		1	
Infection at time of delivery (e.g., influenza)	11		2	
Syphilis	1		1	
Disproportion, etc. (artificial induction)	6		0	
Multiple births	224	22·1	19	22·6
Foetal abnormality	8	0·8	1	1·2
Miscellaneous	6	0·6	2	2·4
Cause not known	419	41·4	25	29·8
Total	1,011	100·0	84	100·0

* 151 pre-eclampsia toxaemia, 18 pre-eclampsia toxaemia+toxic A.P.H., 6 maternal hypertension, 1 maternal nephritis, 1 polyarteritis nodosa with pre-eclampsia, 48 pre-eclampsia in twin pregnancy toxaemia.

Bleeding During Pregnancy (Threatened Abortion).—There were 115 babies whose mothers had a history of bleeding during pregnancy—that is, bleeding other than that occurring immediately before birth (Table II). In this group 17 babies were affected with retinopathy (14.8%). In the 976 cases without bleeding during pregnancy there were 67 babies with a retinopathy (6.9%). The difference is statistically significant. It is due partly, but not wholly, to the differing distribution of birth weights in the two groups, for Table II shows that relatively more of the babies whose mothers had bleeding during pregnancy were under 3½ lb. (1,600 g.)—that is, belonged to those weight groups in which retinopathy is more apt to develop (see below). There is, however, some excess of affected babies at each birth weight,

TABLE II.—*Bleeding During Pregnancy (Threatened Abortion)*

Birth Weight in lb.	No Bleeding During Pregnancy			Bleeding During Pregnancy		
	Total Babies*	Affected Babies	% Affected	Total Babies	Affected Babies	% Affected
Under 3 ..	179	27	15·1	35	7	20·0
3– ..	254	27	10·6	44	8	18·2
3½–4 ..	543	13	2·4	36	2	5·6
Total ..	976	67	6·9	115	17	14·8

* Four babies with cataract omitted.
Metric equivalents for tables: 2½ lb. = 1,150 g.; 3 lb. = 1,350 g.; 3½ lb. = 1,600 g.; 4 lb. = 1,800 g.

suggesting a real association with the occurrence of bleeding during pregnancy. Some previous authors have made the same observation (Ingalls, 1948; Klien, 1949; Szewczyk, 1952), but others not (Gilger, 1949; Kinsey and Zacharias, 1949; Unsworth, 1949; Speert *et al.*, 1950). In the present data, moreover, this association with bleeding during pregnancy appears to link up with the fact that in the affected baby group there was a slight excess of babies whose mothers had had an ante-partum haemorrhage of unknown origin (Table I).

Other Factors in Pregnancy.—The available data on parity, maternal diet (including vitamin supplements), weight gain, and medication could not be usefully analysed, but other workers (Unsworth, 1949; Speert *et al.*, 1950) showed that they were irrelevant.

History of Labour.—A large proportion of the babies were admitted to the nurseries from home, and insufficient detail was available as regards the course of labour or drugs administered to make analysis of any value. It has been stated (Unsworth, 1949) that these factors have no influence.

Family History.—One affected baby in the present series had an older sibling who was blind as a result of retrolental fibroplasia. Other workers have found no evidence of hereditary factors (Krause, 1946; Ingalls, 1948; Unsworth, 1949; Ryan, 1952).

Factors in Baby's Life

Month of Birth.—No definite seasonal changes in incidence were found. This is in agreement with the conclusions of other workers (Crosse, 1950; Ryan, 1952).

Sex and Birth Weight.—The incidence of retinopathy for each sex and for four birth-weight levels is shown in Table III. Taking first all affected babies, it will be seen that the males had a very high rate of incidence at birth weights under 3 lb.: of the 69 babies 20 (29.0%) were affected. The incidence drops sharply to 11.5% with male birth weights of 3 to 3½ lb. and to only 3.3% with birth weights of 3½ to 4 lb. With the female babies there is a very different picture. The incidence in the heaviest babies (3½ to 4 lb.) is, as with males, quite low (2.1%), but in the three lighter groups there is no pronounced rise in the proportion affected as one goes down the weight scale; indeed, rather the reverse. Considering next "blind" babies, the incidence rates do not differ materially between the sexes at birth weights of 2½ to 3½ lb., but male babies of under 2½ lb. show a high incidence compared with the females (the numbers involved are, of course, small) and a somewhat higher incidence amongst the babies over 3½ lb. For both sexes combined, the incidence by birth weight does not vary appreciably until 3½ lb. is reached, above which it drops sharply.

Period of Gestation.—Part of the sex differences revealed in Table III may be due to the differing weights of the sexes in relation to maturity. In Table IV an attempt is made to assess this factor by relating the incidence of retinopathy to the estimated period of gestation. The difference between the sexes is less than that described in the preceding section, though the females still do not reveal the very high rate of the most immature males. In both sexes combined, the rising incidence as the prematurity increases is highly significant statistically.

TABLE IV.—*Incidence of Retinopathy in Relation to Maturity (Measured by the Estimated Period of Gestation)*

No. of Days between Actual and Expected Date of Delivery	Males			Females			M and F
	Total Babies	Affected Babies	%	Total Babies	Affected Babies	%	%
Under 40	105	2	1·9	183	5	2·7	2·4
40– ..	62	3	4·8	92	6	6·5	5·8
50– ..	84	5	6·0	122	7	5·7	5·8
60– ..	52	8	15·4	70	10	14·3	14·8
70–119 ..	61	20	32·8	65	6	9·2	20·6
Not stated	(78)	(5)	(6·4)	(117)	(7)	(6·0)	(6·1)
Total	442	43	9·7	649	41	6·3	7·7

Incidence of Illness and Other Conditions in Early Life.—Of the affected babies, 34.5% had some infection reported during the neonatal period, compared with 29.3% of the normal babies. Non-infective illnesses were reported in 16.9% and 21.4%, congenital abnormalities in 4.8% and 6.0%, and angiomatous naevi in 6.5% and 9.5%. In each instance the rate was slightly higher in the affected babies, though the differences were generally small and might to some degree be due to increased care in recording events in those with affected eyes. Variations in the criteria used by different nurseries made the data as regards oedema, jaundice, and haemoglobin levels of little value.

Anoxia At and After Birth.—The question of whether a baby is anoxic is always a vexed one. In the present survey the difficulties were aggravated by the fact that many different persons filled up the forms and had obviously different criteria, since the percentage of babies recorded as suffering from anoxia at birth varied widely between the nurseries. For the purpose of Table V, a baby was taken as having no history of anoxia if the condition was recorded as normal at birth and no respiratory difficulties—for example, grunting or irregular respiration, cyanotic attacks, or sternal recession—were reported in the first week. If, according to the record, the baby showed blue asphyxia at birth *or* had slight respiratory difficulties during the first two days, this was counted as mild anoxia. If there was a

TABLE V.—*Degree of Anoxia At and After Birth in Relation to Weight Level and Development of Retinopathy*

Birth Weight in lb.	All Babies			Affected Babies			% Affected		
	Severe	Mild	None	Severe	Mild	None	Severe	Mild	None
Under 2½	20	14	27	3	3	4	15·0	21·4	14·8
2½– ..	38	43	72	9	6	9	23·7	14·0	12·7
3– ..	61	96	141	12	7	16	19·0	7·3	11·3
3½–4 ..	75	187	317	4	5	6	5·3	2·7	1·9
Total..	194	340	557	28	21	35	14·3	6·2	6·3

TABLE III.—*Incidence of Retinopathy by Birth Weight and Sex*

Birth Weight in lb.	Total No. of Babies*			"Blind" Babies						Total Affected Babies ("Blind" and Regressed)					
				No.			%			No.			%		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
Under 2½ ..	19	42	61	3	1	4	15·8	2·4	6·6	7	3	10	36·8	7·1	16·4
2½– ..	50	102	152	3	9	12	5·9	8·8	7·8	13	11	24	26·0	10·8	15·8
3– ..	130	168	298	10	10	20	7·8	5·9	6·7	15	20	35	11·5	12·4	11·7
3½–4 ..	243	337	580	6	3	9	2·5	0·9	1·6	8	7	15	3·3	2·1	2·6
Total ..	442	649	1,091	22	23	45	5·0	3·5	4·1	43	41	84	9·7	6·3	7·7

* Four babies with cataract omitted.

record of white asphyxia at birth or considerable respiratory difficulties during the first few days of life, or of blue asphyxia at birth *and* respiratory difficulties during the first two days, the baby was counted as severely anoxic. While this classification is open to many criticisms, it should serve to give a broad indication of the presence and degree of anoxia. Taking the all-important factor of birth weight into account, Table V shows (with the small numbers available) that with babies under 2½ lb. the occurrence of anoxia did not affect the incidence of retrolental fibroplasia. At the higher birth weights there was an increased incidence of retinopathy in babies classified as severely anoxic compared with those with mild anoxia or none. Other authors have found an association of anoxia in the infant with the later development of a retinopathy (LeLong *et al.*, 1952).

Not unexpectedly, the incidence of severe anoxia diminishes as the birth weight increases, being 32.8% in the group weighing under 2½ lb., 25.0% in the 2½–3 lb. group, 21.0% in the 3–3½ lb. group, and 12.9% in the 3½–4 lb. group (derived from Table V). This steadily falling incidence does not mirror the incidence of "blind" babies in the weight groups, where it remains more or less constant till a birth weight of 3½ lb. is reached, above which it falls suddenly (Table III).

Consideration of the relation between the cause of prematurity and the recorded incidence of clinical anoxia shows that severe anoxia, as defined above, occurred in 18% of all the babies, in 20% of the offspring of toxaemic mothers, in 18% of those whose mothers had placenta praevia or ante-partum haemorrhage of unknown origin, and in 30% of the offspring of mothers with a history of vaginal bleeding during pregnancy. The last group, it may be recalled, showed a relatively high incidence of retinopathy (Table II), which clearly may be in part due to this significantly more frequent presence of severe anoxia. On the other hand, there would usually be a link between the anoxia shown by a baby and the amount of oxygen given therapeutically.

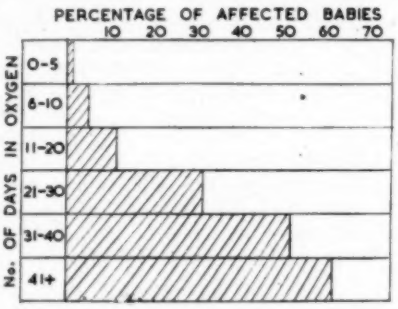


FIG. 1.—Incidence of retinopathy in relation to treatment with oxygen.

Treatment with Oxygen

With regard to oxygen therapy, questions were asked relating to the type of apparatus used (which varied from home-made boxes to the latest models), the rate of flow

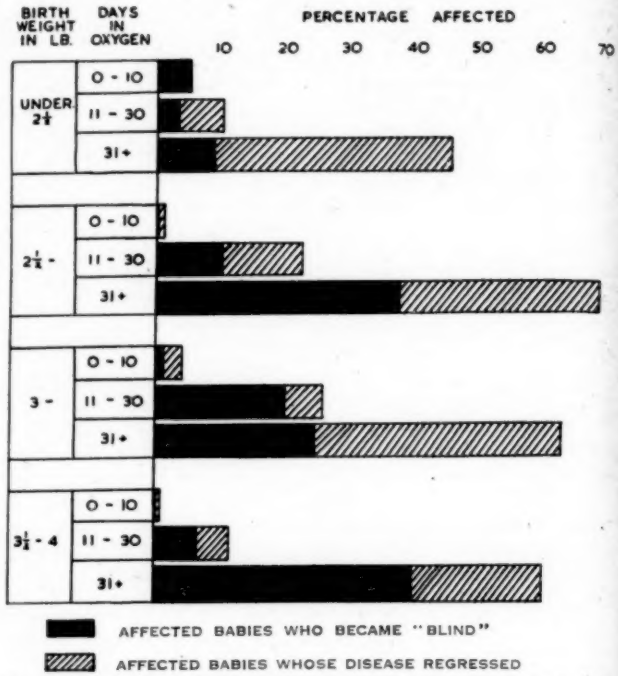


FIG. 2.—Incidence of retinopathy in relation to birth weight and treatment with oxygen.

TABLE VI.—*Incidence of Retinopathy in Relation to Treatment with Oxygen*

No. of Days in Oxygen	Total* No. Babies	Unaffected				"Blind"				Regressed				% Affected ("Blind" and Regressed)
		Birth Weight (lb.)				Birth Weight (lb.)				Birth Weight (lb.)				
		Under 2½	2½–	3–	3½–4	Under 2½	2½–	3–	3½–4	Under 2½	2½–	3–	3½–4	
0	344		18	77	249									0·0
1	61	3	8	11	39									0·0
2	69	3	5	13	46				1			1		2·9
3	58		5	22	31									0·0
4	49	1	6	15	27									0·0
5	47		7	8	29	1		1	1					6·4
6–10	183	12	27	56	78			2			1	5	2	5·5
11–20	154	14	31	40	48	1	3	6	2		5	2	2	13·6
21–30	60	12	13	11	4		3	7	3	2	1	3	1	33·3
31–40	15	2	1	2	2	1	4			1	2			53·3
41–50	14	3		1			2	2	1	1	2	2		
51–60	6		2						1		1	1	1	
61–70	2	1	1											64·0
71–80	2									2				
81–90	1		1											
Not stated	26		3	7	12	1		2				1		
Total	1,091	51	128	263	565	4	12	20	9	6	12	15	6	
Mean No. of days in oxygen ..		17·7	11·3	6·5	3·6	18·7	29·7	21·3	23·9	47·2	27·4	21·1	21·3	

* Four babies with cataract omitted.

TABLE VII.—*Incidence of Retinopathy in Relation to Treatment with Oxygen*

No. of Days in Oxygen	Total Babies*				% Affected ("Blind" and Regressed)				% "Blind"			
	Birth Weight (lb.)				Birth Weight (lb.)				Birth Weight (lb.)			
	Under 2½	2½–	3–	3½–4	Under 2½	2½–	3–	3½–4	Under 2½	2½–	3–	3½–4
10 or less ..	20	77	211	503	5·0	1·3	4·3	0·8	5·0	0·0	1·4	0·4
11–30 ..	29	57	69	59	10·4	22·8	26·1	11·9	3·4	10·5	20·3	6·8
31 or more ..	11	16	8	5	45·5	68·8	62·5	60·0	9·1	37·5	25·0	40·0

* Four babies with cataract omitted. Twenty-six omitted for whom the number of days in oxygen was not stated.

and concentration attained, the method of withdrawing oxygen (asked on some later forms only), and the length of time that the baby was in oxygen. The last question was answered in nearly all cases, and is the only one that proved suitable for statistical analysis.

The basic data regarding this factor are shown in Tables VI and VII and Figs. 1 and 2. It will be seen that of the 344 babies who had no oxygen (mainly the heavier babies), none developed a retinopathy. Of all babies with less than five days of oxygen treatment (581), only two were affected, one regressively and one progressively.

The latter was a baby of 3 lb. 13 oz. (1,730 g.) birth weight who had two days in oxygen; it was an atypical case which presented with generalized oedema and glaucoma, and it was only after several weeks, when the corneal oedema had subsided, that the changes of a retinopathy became apparent; no retrolental membrane was ever formed. Likewise in the case that regressed, the baby had two days of oxygen treatment; the retinopathy was a very mild neovascularization which subsided without treatment.

The right-hand column of Table VI and Fig. 1 show a steeply rising incidence with increasing length of oxygen treatment. Thus the proportion affected ("blind" and regressed) was approximately 1 in 50 of the 811 babies given oxygen for 10 days or less, 1 in 5 of the 214 babies given oxygen for 11–30 days, and 3 in 5 of the 40 babies given oxygen for 31 days or more. The corresponding proportions for "blind" babies were, roughly, 1 in 130, 1 in 9, and 1 in 4. The bottom line of Table VI shows the average length of time spent in oxygen. The unaffected babies of a birth weight of 2½ lb. or more had averages of *4 to 11 days* in oxygen (the duration falling with increasing birth weight); the corresponding affected babies (both "blind" and regressed) had averages of *3 to 4 weeks*. The incidence rates in relation to birth weight and increasing treatment with oxygen are shown in Table VII and Fig. 2. Within each weight group the percentage of babies affected increased greatly with longer treatment. Other authors have found an association between oxygen treatment and retinopathy of prematurity (Campbell, 1951; Crosse, 1951; Jefferson, 1952; Patz *et al.*, 1952; Ashton *et al.*, 1953, 1954).

Oxygen Therapy in Relation to Anoxia.—It may be argued that babies who develop a retinopathy do so because they are ill in the first place and, in particular, anoxic. They therefore require more oxygen, but it may be the illness rather than excessive oxygen that is the direct cause of the retinopathy. Figures bearing on this point are given in Table VIII. It will be seen that babies with severe anoxia did, on the average, get more oxygen, and a higher proportion of them spent five or more days in oxygen. At birth weights of 2½ lb. and over the babies with severe anoxia had a higher incidence of retinopathies. On the other hand, it is apparent that the babies with mild or no anoxia at or after birth had a quite substantial incidence, the proportions affected in the lighter weight-groups being 17.1%, 13.9%, and 9.7%. In other words, many babies who were not clinically anoxic subsequently developed a retinopathy.

TABLE VIII.—*Degree of Anoxia in Relation to Duration of Treatment with Oxygen and Incidence of Retinopathy*

	Severe Anoxia	Mild or No Anoxia
Under 2½ lb.:		
Mean No. of days in oxygen	22·9	19·5
% with 5 or more days in oxygen	94·7	85·4
No. of babies	20	41
% affected ("blind" and regressed)	15·0	17·1
2½–:		
Mean No. of days in oxygen	16·9	12·2
% with 5 or more days in oxygen	81·6	69·6
No. of babies	38	115
% affected ("blind" and regressed)	23·6	13·9
3–:		
Mean No. of days in oxygen	11·2	7·3
% with 5 or more days in oxygen	68·9	39·2
No. of babies	61	237
% affected ("blind" and regressed)	19·7	9·7
3½–4:		
Mean No. of days in oxygen	7·5	3·6
% with 5 or more days in oxygen	62·7	25·8
No. of babies	75	504
% affected ("blind" and regressed)	5·3	2·0

Oxygen Therapy, Retinopathy, and Survival Rate.—The incidence of retinopathy in four broadly contrasting groups of nurseries is shown in Table IX, in relation to their use of oxygen and the survival rates of the babies entering them. Except in the lightest weight group, the average time the babies spent in oxygen decreases as the incidence of progressive retinopathies in the nurseries decreases from 10% to nil. The percentages of babies surviving for at least two months do not show that those nurseries in which more oxygen was given had a better survival rate. Nor do the figures (not given in Table IX) for babies dying between the ages of 3 days and 2 months show that the increased use of oxygen favourably affected the mortality rate between these ages. The mortality rate was 14% for nurseries in group 1, 8% for group 2, 12.4% for group 3, and 8.9% for the group in which no case of "blindness" occurred. The corresponding incidence rates of all retinopathies ("blind" and regressed) for the four groups of nurseries were 21.6%, 9.9%, 5.8%, and 1.5%.

TABLE IX.—*Incidence of "Blindness" in Different Nurseries in Relation to Use of Oxygen and Survival Rate*

Birth Weight in lb.	Survival Rate and Days in Oxygen	Group 1 (3 Nurseries)	Group 2 (3 Nurseries)	Group 3 (7 Nurseries)	Group 4 (4 Nurseries)
		Incidence of "Blindness"			
		Over 10%	5–9%	1–4%	No "Blindness"
Under 2½	Total admitted	48	69	198	102
	% survivals*	8·3%	19·0%	13·6%	19·0%
	Av. days in oxygen	6·5	21·1	18·0	14·3
2½–	Total admitted	44	72	129	83
	% survivals*	47·7%	57·0%	42·7%	42·1%
	Av. days in oxygen	31·7	13·1	11·7	5·0
3–	Total admitted	72	108	190	116
	% survivals*	66·7%	56·4%	64·5%	60·0%
	Av. days in oxygen	16·1	10·5	5·5	2·5
3½–4	Total admitted	103	161	297	207
	% survivals*	73·0%	79·0%	76·0%	73·6%
	Av. days in oxygen	7·4	7·3	2·7	2·0
Total No. of babies admitted		267	410	814	508

* Babies surviving two months or more.

Factors Contributing to Regression of Retinopathy

Time in Oxygen.—The time in oxygen does not appear to be a factor in regression, since the mean durations at each weight for the "blind" and the regressed were very similar (see Table VI). For all weights combined, the mean duration was 24 days for the "blind" and 27 days for the regressed. Similarly, there is no clear difference between the four groups of nurseries of Table IX. In the nurseries with the highest rate of retinopathy (and using oxygen most freely) 47% of the cases regressed, while in the following two groups the proportions were 30% and 52%. In group 4 (using least oxygen) four cases were reported and all regressed. One difficulty is that the diagnosis of regressive cases may vary from one nursery to another according to the frequency with which the babies' eyes were examined.

Withdrawal of Oxygen.—The method of withdrawing oxygen was not known in many instances, but the figures, for what they are worth, reveal no difference between the "blind" and regressed cases.

Sex and Maturity.—The sexes have similar proportions of cases that regressed—48.8% male and 43.9% female. Table X suggests that the more premature babies had a better chance of regression.

Feeding.—Only babies under 3½ lb., with their relatively high incidence of the disease, were used for this study.

TABLE X.—*Maturity, Sex, and Regression*

No. Days Prematurity	Total Retinopathy		Regressing Cases		% Regressing	
	M	F	M	F	M	F
Under 60 ..	10	18	4	8	40	44
60–	8	10	4	4	50	40
70 or over ..	20	6	11	4	55	67
Not stated ..	(5)	(7)	(2)	(2)		
Total ..	43	41	21	18	49	43

They were divided into three groups : (1) those who had breast milk for at least 35 days after birth, (2) those who were changed to artificial feed between the 24th and 34th day of life, and (3) those who had artificial feed before the 24th day. The incidence of retinopathy was approximately similar in all three groups. On the small amount of data available the numbers showing regression were 28 out of 48 cases (58.3%) in group 1, 2 out of 6 (33.3%) in group 2, and 2 out of 15 (13.3%) in group 3.

Clinical Features of the Retinopathy

Time of Onset.—The time at which the retinopathy appears has been variously thought to depend on the birth weight of the baby, taking longer to appear in lighter babies (LaMotte, 1951), or else to be related to the discontinuation of oxygen, dilated and tortuous vessels appearing within a few days (Szewczyk, 1952 ; Ashton *et al.*, 1953, 1954).

In the present series the average time of onset of the retinopathy in all the affected babies in each weight group is given in Table XI. These figures suggest that the more

TABLE XI.—*Average Age at Onset of Retinopathy*

Birth Weight in lb.	Average No. of Days in Oxygen of All Affected Babies	Average Age at Onset of Retinopathy (Days)	Average Interval Between End of Oxygen and Recognition of Retinopathy (Days)	No. of Babies in Group and No. in Whom Time of Onset was Not Known
Under 2½	22	56	34	2/10
2½– ..	27	46	19	2/24
3– ..	20	33	13	5/35
3½–4 ..	18	27	9	2/15

premature the baby at birth the longer delayed, on the average, will be the onset of the retinopathy ; and also, that the time of the appearance of the first ophthalmic sign is not dependent alone on the time of withdrawal from oxygen.

Ophthalmoscopic Appearances

The changes in active and cicatricial retinopathy of prematurity have been well described and illustrated in the *American Journal of Ophthalmology* (Anon., 1953). Of the 39 cases which regressed in the present series, 24 showed neovascularization and peripheral oedema only ; 11 showed minor peripheral detachments as well ; and 4 showed quite extensive detachments which returned to normal. (One of the latter 4 children had, in addition to a detachment, extensive haemorrhage into the vitreous with fronds of vessels growing into it. This baby became completely normal, and it was difficult to believe it could be the same child.) Of the 45 progressive cases, 18 had bilateral complete membranes and 11 were babies showing a complete membrane in one eye. The other eye was normal in 2 babies, had some local peripheral scarring in 1, and in the other 8 partial detachment, fibrous bands, myopia, and atrophic disks and retinae were seen. Of the remaining 16 cases which progressed, 3 had detachments in one or both eyes, the other eye having an atrophic retina ; 6 had bilateral changes, including atrophic retinae, atrophic disks, and myopia ; 2 had fibrous bands across their retinae, the other eye being normal ; and 1 had an atrophic retina in one eye, the other being normal ; the 4 other babies died, and all showed bilateral detachments at various stages of development.

Treatment of the Retinopathy

Treatment by return to oxygen or the use of corticotrophin was tried, but no conclusive results concerning the value of either were obtained owing to the small number of babies treated. The chances of regression without treatment were 44% in the present series.

Summary

This study of retrolental fibroplasia included 1,095 babies in the United Kingdom weighing 4 lb. (1,800 g.) or under at birth and surviving at least two months, 84 of whom were affected with retinopathy. The following conclusions emerge.

1. The cause of prematurity, and maternal factors other than vaginal bleeding, did not influence the subsequent development of the disease.

2. Boys were more often affected than girls ; the main reason for this appears to be that they are more immature than girls for a given birth weight.

3. The nurseries showed wide variations in their use of oxygen and, in general, corresponding variations in the incidence of the disease.

4. The use of oxygen predisposed to the development of a retinopathy. Except in two cases, at least five days' treatment with oxygen was required to produce the disease ; and the likelihood of a baby getting the disease increased as the treatment with oxygen was prolonged.

5. There are many other variables to be taken into account, but nurseries in which little oxygen was given, and which were free from cases of progressive retinopathy, did not, on the average, experience survival rates inferior to nurseries using more oxygen.

6. Clinical signs of anoxia at and after birth were associated with a higher incidence of retinopathy, but on the average more oxygen was given to anoxic babies.

REFERENCES

Anon. (1953). *Amer. J. Ophthal.*, **36**, 1334.
Ashton, N., Ward, B., and Serpell, G. (1953). *Brit. J. Ophthal.*, **37**, 513.
—— —— —— (1954). Ibid., **38**, 397.
Campbell, K. (1951). *Med. J. Aust.*, **2**, 48.
Crosse, V. M. (1950). *Proc. roy. Soc. Med.*, **43**, 232.
—— (1951). *Trans. Ophthal. Soc. U.K.*, **71**, 609.
Gilger, A. P. (1949). *Amer. J. Ophthal.*, **32**, 917.
Ingalls, T. H. (1948). *Pediatrics*, **1**, 315.
Jefferson, E. (1952). *Arch. Dis. Childh.*, **27**, 329.
King, M. J. (1950). *Arch. Ophthal. (Chicago)*, **43**, 694.
Kinsey, V. E. (1951). *M. & R. Paediatric Research Conference Report*, p. 37. New York.
—— and Zacharias, L. (1949). *J. Amer. med. Ass.*, **139**, 572.
Klien, B. A. (1949). *Arch. Ophthal. (Chicago)*, **41**, 553.
Krause, A. C. (1946). Ibid., **36**, 387.
LaMotte, W. O., jun. (1951). *M. & R. Pediatric Research Conference Report*, p. 26. New York.
LeLong, M., Rossier, A., Fontaine, M., LeMasson, C., Michelin, J., and Audibert (1952). *Arch. franç. Pédiat.*, **9**, 897.
Patz, A., Hoeck, L. E., and De la Cruz, E. (1952). *Amer. J. Ophthal.*, **35**, 1248.
Platou, R. V. (1951). *M. & R. Pediatric Research Conference Report*, p. 33. New York.
Ryan, H. (1952). *Amer. J. Ophthal.*, **35**, 329.
Speert, H., Blodi, F. C., and Reese, A. B. (1950). *Amer. J. Obstet. Gynec.*, **59**, 246.
Szewczyk, T. S. (1952). *Amer. J. Ophthal.*, **35**, 301.
Terry, T. L. (1942a). Ibid., **25**, 203.
—— (1942b). Ibid., **25**, 1409.
Unsworth, A. C. (1949). *Trans. Amer. Ophthal. Soc.*, **47**, 738.

Speaking from the new offices of the Medical Sickness, Annuity and Life Assurance Society at 3, Cavendish Square, London, W.1, Mr. R. J. MCNEILL LOVE told the 70th annual general meeting on June 7 that the funds of the Society now totalled over £6m. The Sickness and Insurance Fund, limited to medical and dental practitioners, was now over £2m., and during 1954 1,300 new sickness contracts had been signed.

INCIDENCE OF RETROLENTAL FIBROPLASIA IN ENGLAND AND WALES IN 1951

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In 1952, on behalf of the Ministry of Health, we initiated an inquiry into the incidence and distribution of retrolental fibroplasia in England and Wales. At that time, all that was known with certainty about the disease was that it affected the smaller premature infants and that its geographical distribution was erratic.

Medical officers of health in England and Wales are aware of all live births in their areas that are premature, as defined by the internationally accepted birth-weight standard, since, from 1946 onwards, doctors and midwives have been asked to enter the birth weight of a live-born infant on the birth notification whenever the weight is 5½ lb. (2,500 g.) or less. (More recently the entry of the birth weight of babies of all weights, live-born and stillborn, has been requested.) On the basis of this information the medical officer of health of every local health authority was asked to make special inquiry about the condition of eyes of all the premature infants born in 1951 whose birth weight was not more than 4 lb. 6 oz. (2,000 g.) and who had survived at least two months—that is, those premature infants who were at risk by reason of low birth weight and who had survived long enough to demonstrate retrolental fibroplasia.

The inquiry was carried out by health visitors in the first place, and through them information was sought on birth weight, sex, place of birth (home or hospital), whether transferred to hospital after birth at home, whether single or multiple birth, and, in broad terms, on the condition of the eyes. Since all the infants were at least 10 months old when the inquiry started, seriously defective vision would have been apparent to the parents and the health visitors. In many cases of defective vision it was already known that the child was, or had been, under the care of an ophthalmologist, and an accurate diagnosis was thus readily obtained. In cases of doubt the co-operation of the family doctor and the ophthalmologist was sought and retrolental fibroplasia excluded or confirmed on expert opinion, sometimes after a period of observation and repeated examinations. By these means the details of the babies born, and information on the cases of retrolental fibroplasia occurring among them, were received from every local health authority.

Incidence in Relation to Birth Weight

In total the survey provided data on 6,926 infants, all of whom had weighed 4 lb. 6 oz. or less at birth, and who had survived for a period of at least two months. The distribution of these infants by place of birth, sex, and birth weight (Table I) showed that the great majority of them, 6,042 (87%), had either been born in hospital (or nursing-home) or were transferred there within two months; 797 infants (12%) were born at home and were not transferred; while the information regarding place of birth was incomplete for the remaining 87 (1%). There was a considerable excess of females among the total infants, and this excess became relatively larger with each successive decrease in birth weight.

The condition of the eyes was ascertained in all but 295 babies (4.3%), who either could not be traced or had left the country. These have been presumed normal. Among the total population of 6,926 infants 127 cases of retrolental fibroplasia were discovered, an incidence rate of 1.83% for infants of 4 lb. 6 oz. (2,000 g.) or lower birth weight. (For infants with a birth weight of 4 lb. (1,800 g.) or less the rate was 2.8%.) Detailed analysis of the incidence by birth weight (Table II) reveals a marked fall with increasing birth weight; a rate of 15.3% in infants whose birth weight had been under 2 lb. 4 oz. (1,000 g.) declines steadily to a rate of only 0.2% in infants with a birth weight between 3 lb. 14 oz. and 4 lb. 6 oz. (1,750 and 2,000 g.).

TABLE II.—*Incidence of Retrolental Fibroplasia Among* 6,926 *Premature Infants Born in England and Wales During* 1951

Birth Weight	No. of Infants	Cases of Retrolental Fibroplasia	
		No.	Incidence Rate %
Under 2 lb. 4 oz. (1,000 g.)	85	13	*15·3*
2 lb. 4 oz. (1,000 g.)– ..	302	40	*13·3*
2 „ 13 „ (1,250 „)– ..	867	36	*4·2*
3 „ 5 „ (1,500 „)– ..	1,790	30	*1·7*
3 „ 14 „–4 lb. 6 oz. (1,750–2,000 g.) ..	3,882	8	*0·2*
Total	6,926	127	*1·8*

Incidence in Relation to Place of Birth

All the 127 cases of retrolental fibroplasia occurred among the 6,042 infants who were born in hospital or were transferred there within two months, and none of the 797 who were born at home and remained there for the first two months of life developed the disease. This absence of cases among the "home" infants supports the view that the risk

TABLE I.—*Numbers of Premature Infants* Born in England and Wales During* 1951, *by Place of Birth and Birth Weight*

Birth Weight	Born in Hospital (or Nursing-home) or Transferred there within 2 Months			Born at Home and not Transferred to Hospital (or Nursing-home)			Place of Birth, or Subsequent Transfer Not Known			Total			
	M	F	Sexes Combined	M	F	Sexes Combined	M	F	Sexes Combined	M	F	Sexes Combined	M : F Ratio
Under 2 lb. 4 oz. (1,000 g.)..	23	58	81	2	2	4	0	0	0	25	60	85	42 : 100
2 lb. 4 oz. (1,000 g.)– ..	106	186	292	4	6	10	0	0	0	110	192	302	57 : 100
2 „ 13 „ (1,250 „)– ..	356	448	804	17	37	54	5	4	9	378	489	867	77 : 100
3 „ 5 „ (1,500 „)– ..	731	904	1,635	70	68	138	4	13	17	805	985	1,790	82 : 100
3 „ 14 „–4 lb. 6 oz. (1,750–2,000 g.)	1,511	1,719	3,230	247	344	591	26	35	61	1,784	2,098	3,882	85 : 100
Total	2,727	3,315	6,042	340	457	797	35	52	87	3,102	3,824	6,926	81 : 100

* Infants whose birth weight was 4 lb. 6 oz. (2,000 g.) or less, and who survived two months or more.

of developing retrolental fibroplasia is closely associated with some factor connected with hospitalization. Applying the specific incidence rates by sex and birth weight observed in the total population of infants to the number of infants in each of the corresponding subgroups of the "home" population, it is found that as many as seven or eight cases would have occurred among the infants born at home and not transferred to hospital, if they had been subject to the same risks as the whole population. Making due allowance in this way for the differing sex and birth-weight compositions of the two groups, the incidence of retrolental fibroplasia in "hospital" infants can be directly compared with that in "home" infants. The difference between them is significant ($\chi^2 = 8.14$, n = 1, $P < 0.01$).

TABLE III.—*Incidence of Retrolental Fibroplasia Among Infants Born in or Transferred to Hospital (or Nursing-home)*

Birth Weight	Males			Females			Sexes Combined		
	No. of Infants	Cases of R.F.		No. of Infants	Cases of R.F.		No. of Infants	Cases of R.F.	
		No.	Rate %		No.	Rate %		No.	Rate %
Under 2 lb. 4 oz. (1,000 g.) ..	23	3	13·0	58	10	17·2	81	13	16·1
2 lb. 4 oz. (1,000 g.)– ..	106	20	18·9	186	20	10·8	292	40	13·7
2 lb. 13 oz. (1,250 g.)– ..	356	23	6·5	448	13	2·9	804	36	4·5
3 lb. 5 oz. (1,500 g.)– ..	731	21	2·9	904	9	1·0	1,635	30	1·8
3 lb. 14 oz.–4 lb. 6 oz. (1,750–2,000 g.) ..	1,511	7	0·5	1,719	1	0·06	3,230	8	0·3
Total ..	2,727	74	2·7	3,315	53	1·6	6,042	127	2·1

The overall incidence rate of the disease among infants born in or transferred to hospital, and with a birth weight not exceeding 4 lb. 6 oz. (2,000 g.), was 2.1 per 100 infants (Table III). It is of some interest to consider the incidence amongst the "hospital" infants with a birth weight not exceeding 4 lb. (1,800 g.). In these babies the incidence was 3.2%, a figure which may be compared with the 4.1% of "blind" babies observed in the Medical Research Council's inquiry (1955).

Incidence in Relation to Sex

Examination of the incidence in different birth-weight groups and for males and females separately (Table III) reveals two definite features. For each sex there is a pronounced decline in the incidence rates from the lower to the higher birth-weight groups (as has already been demonstrated for all infants in Table II). Secondly, the total incidence rate for males (2.7%) is considerably higher than that for females (1.6%), and with one exception there is a consistently higher male incidence in the separate birth-weight groups. The one exception occurred amongst the infants with the lowest birth weights (less than 2 lb. 4 oz.) (1,000 g.), where the female incidence rate was somewhat higher than that for males. The number of male infants in this birth-weight group was, however, small (only 23).

Comparison of the incidence in males and females, after due allowance for their differing birth-weight distributions, gives a highly significant difference ($\chi^2 = 17.20$, n = 1, $P < 0.001$). This difference does not necessarily establish sex, *per se*, as a factor affecting the incidence rate of the disease. It may well be a reflection of differing levels of maturity among the male and female infants. Female infants have lower birth weights than male infants of the same maturity, and male infants suffer a higher neonatal mortality in each of the birth-weight groups adopted here (Shapiro, 1954). Thus the fixing of an arbitrary upper limit of birth weight for the survey may have been responsible in part for the high female : male ratio of infants observed, and, as a corollary, may have caused the proportion of more immature infants to be greater among the males.

The effect of maturity on the comparison between the sexes can be at least partially eliminated by comparing the incidence among equal numbers of males and females at the lower end of the birth-weight scale. If, for example, the first 500 infants in each sex are chosen consecutively in ascending order of birth weight, the two groups so constituted should be reasonably similar in their levels of maturity. It can be estimated from Table III that the first 500 males have birth weights up to 3 lb. 5 oz. (1,500 g.) and the first 500 females birth weights up to 3 lb. 2 oz. (1,420 g.). The numbers of cases of retrolental fibroplasia with birth weights up to these levels were 47 males and 38 females. The difference is not statistically significant. It may well be, therefore, that the higher incidence among the male infants is largely a reflection of their lower level of maturity as compared with the female infants.

Incidence in Relation to Multiple Births

Of the infants included in this survey, 2,191 (36%) came from multiple births, and were made up of 2,077 twin babies, 105 members of triplets, and 9 members of quadruplets. From the triplets four infants and from the quadruplets three infants developed retrolental fibroplasia. Details of the incidence of the disease in twins are given in Table IV,

TABLE IV.—*Incidence of Retrolental Fibroplasia Among* 2,077 *Twins Born in England and Wales During* 1951

Birth Weight	All Twins			Twins Born in Hospital or Transferred to Hospital (or Nursing-home) within 2 Months		
	No. of Infants	Cases of R.F.		No. of Infants	Cases of R.F.	
		No.	Rate %		No.	Rate %
Under 2 lb. 4 oz. (1,000 g.) ..	17	3	17·7	16	3	18·8
2 lb. 4 oz. (1,000 g.)–	64	7	10·9	60	7	11·7
2 lb. 13 oz. (1,250 g.)–	260	16	6·2	233	16	6·9
3 lb. 5 oz. (1,500 g.)–	578	13	2·3	521	13	2·5
3 lb. 14 oz.–4 lb. 6 oz. (1,750–2,000 g.)..	1,158	0	0	940	0	0
Total	2,077	39	1·9	1,770	39	2·2

which shows that there were 39 cases, giving an overall rate of 1.9% and a hospital rate of 2.2%. Both these figures are in close agreement with the corresponding rates for all infants (1.8% and 2.1%). The same pattern of a marked decline in incidence of the disease with increasing birth weight was present among twins, and the incidence rates in the different birth-weight groups are similar to the corresponding rates for all infants.

Incidence in Relation to Region

The local health authorities were grouped into 11 regional areas and the incidence rates of retrolental fibroplasia in each of these areas obtained. Two measures of incidence were calculated for each region—a crude incidence rate based on all infants whose birth weight was not more than 4 lb. 6 oz. (2,000 g.), and an incidence rate based on infants

TABLE V.—*Incidence of Retrolental Fibroplasia in Different Regions of England and Wales* (1951)

Region	Incidence Rates (%)	
	All Infants	Infants Born in or Transferred to Hospital (or Nursing-home)
Northern	1·33	1·84
East and West Ridings..	1·05	1·15
North Midlands ..	2·03	2·39
Eastern	1·62	1·84
London	1·70	1·81
Southern	1·46	1·73
South-western ..	2·14	2·50
Wales	2·49	2·86
Midlands	0·89	1·04
North-western	2·74	3·07
South-eastern	2·45	2·75
England and Wales ..	1·83	2·10

of the same birth weights born in hospital or transferred there within two months of birth. Both measures show a considerable variation between different parts of the country (Table V). The experience of the Midlands region was the most favourable (all infants 0.89%, "hospital" infants 1.04%), and the highest incidence occurred in the North-western region (all infants 2.74%, "hospital" infants 3.07%).

Neither of these crude measures of incidence makes any allowance for possible differences in the sex and birth-weight distribution of infant populations in the different regions. The pattern of variation displayed by the crude rates can, however, be confirmed by a measure of incidence which makes adjustment for such differences. Thus the sex and birth-weight specific incidence rates for the whole country ("hospital" infants) were applied to the "hospital" infants of each region to give the number of infants "expected" to have developed the disease had there been no regional variation. Expressing the number of cases observed as a proportion of the "expected" number provides an index making appropriate allowance for differing sex and birth-weight distributions of the populations (Table VI). The wide

TABLE VI.—*Incidence in Each Region Compared with Incidence in England and Wales as a Whole (Based on Infants Born in or Transferred to Hospital or Nursing-home Within Two Months)*

Region	Relation Between Incidence and that of All E. and W.
Midlands	52% lower
East and West Ridings	43% "
London	25% "
Eastern	16% "
Southern	14% "
Northern	6% "
North Midlands	2% "
South-eastern	16% higher
South-western	27% "
Wales	60% "
North-western	65% "

variation between different regions was again apparent, with an incidence ranging from about 50% lower to more than 50% higher than that experienced over the whole of England and Wales. All three measures of incidence showed the rates to be highest in the North-western and Welsh regions and lowest in the Midlands and East and West Riding regions.

Summary

Particulars have been obtained from all local authorities in England and Wales of infants born in 1951 having a birth weight of 4 lb. 6 oz. (2,000 g.) or less and surviving at least two months. Of 6,926 such infants, 1.83% had retrolental fibroplasia. No case was found amongst the 797 infants born at home and never transferred to hospital. The incidence was closely related to birth weight, declining steeply with increasing birth weight. The incidence was higher in males than in females, but this difference may be due to male babies being less mature than female babies of the same weight. Twin babies showed the same incidence as single babies. Considerable regional variability was observed, with relatively high rates in Wales and the North-western counties and low rates in the Midlands and East and West Ridings of Yorkshire.

We are grateful to Professor A. Bradford Hill for helpful advice and criticism in the planning of the survey and in the preparation of this report. We are also deeply indebted to the medical officers of health, whose assistance enabled the survey to comprise the whole of England and Wales, to the many health visitors who compiled the detailed returns, and to the ophthalmologists who so readily co-operated.

REFERENCES

Medical Research Council Report (1955). *British Medical Journal*, 2, 78.
Shapiro, S. (1954). *Amer. J. publ. Hlth.* 44, 1142.

HEREDITARY COPROPORPHYRIA

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In 1936 Dobriner reported a case in which a woman excreted large amounts of coproporphyrin (probably series III) and traces of uroporphyrin in the urine, and also large amounts of coproporphyrin (series I and III) and protoporphyrin in the stool. Although this woman was then a patient in a psychiatric ward, there were no apparent symptoms associated with the abnormal porphyrin excretion. Watson *et al.* (1949) described the cases of two men who excreted large amounts of coproporphyrin III in the urine and stools, unaccompanied by symptoms. They stated that this condition, which they called "idiopathic coproporphyrinuria," represented an "inborn error of metabolism," although they could not find evidence for any hereditary association of the abnormality.

The present paper describes the occurrence of a similar pigment disturbance in a Swiss boy, in his mother and father (who are first cousins), and also in his paternal aunt. The boy excretes much higher quantities of coproporphyrin in his urine and faeces than the others and also passes traces of uroporphyrin I in his urine. He has suffered from rickets, noted for the first time at 3½ years, as well as from riboflavine deficiency. An unusual amino-acid excretion pattern was obtained by paper chromatography in three of these four subjects. The term "hereditary coproporphyria" has been used for this condition, because of the genetic significance of these findings and because the porphyrins are excreted in the faeces as well as in the urine, principally in the faeces.

Methods

Porphyrins.—Quantitative determinations of porphyrins and porphobilinogen in the urine and stools were carried out as in a previous study (Goldberg, 1954). Since initial investigation had shown that the excess porphyrins were entirely ether-soluble, the isolation and identification were done as under "ether-soluble porphyrins."

Urinary amino-acids were identified by paper chromatography (Dent, 1951).

Riboflavine determinations were carried out by means of microbiological assay, using *Lactobacillus casei*, or fluorimetrically.

Case Report

This patient was born in 1944 after a normal labour. His mother had hyperemesis during pregnancy. Birth weight, 3 kg. He was breast-fed until the age of 7 months, then was given breast milk and vegetables until 1 year, when he was put on a mixed diet. His first tooth erupted at 1 year and he completed his primary dentition by the end of his second year. He started walking at 1½ years and spoke his first word at 2. About the age of 1½ years he had a generalized skin rash, which disappeared when milk was discontinued. About this time he also had diarrhoea, which was treated in the out-patient department of the Jenner-Kinderspital, Berne, Switzerland. At 3½ years he had a severe middle-ear infection, which later was complicated by a throat and lung infection. He recovered from

this, but one month later developed gastro-enteritis with marked dehydration. At this time his family doctor noted that he had rickets and gave him calcium and vitamin preparations without benefit. At 4 years his mother observed that some of his nails were cracked and heaped up and that there was "eczema" between his fingers, where infection was common. There was also some cracking and irritation of the buccal mucous membrane and at the angles of the mouth. His mother believed that when he drank milk his mouth and hands got worse. His skin had never been affected adversely by the sun.

On September 22, 1952, he was admitted to the Jenner-Kinderspital under the care of Professor Ed. Glanzmann because of further attacks of diarrhoea and also for treatment of his rickets, mouth, and nails. It was during this admission that an investigation of the urine disclosed the incidental presence of excessive porphyrins.

FIG. 1

FIG. 2

FIG. 3

FIG. 1.—The patient, showing presence of rickets. FIG. 2.—Forearms and hands of patient before treatment. FIG. 3.—Forearms and hands after one year of treatment.

Physical examination showed a normally intelligent boy with rickets (Fig. 1), undersized and underweight for his age. He was 108 cm. in height, 18.5 kg. in weight, while the standard height and weight for his age were 123 cm. and 24.4 kg. respectively. There was slight hypertelorism. The thorax was funnel-shaped, with a marked rachitic rosary. There was thickening of the epiphysial ends of the long bones, shortening and bowing of the femur, and antero-lateral bending of the tibiae. There was marked cheilosis and the tongue was red, shiny, and without papillae. His skin was generally dry, scaly, and hyperkeratotic, and there was also hyperkeratosis of the nails. Examination of his eyes showed a bilateral granular and flocculent cataract, denser centrally and finer more peripherally. He was hypermetropic. There was no further abnormality on physical examination; in particular, the liver and spleen were not enlarged. His blood pressure was 125/60. Chvostek's and Trousseau's signs were negative.

Tests

Peripheral Blood.—Hb 78%; R.B.C., 4,000,000 per c.mm., reticulocytes, 0.6%; platelets, 150,000 per c.mm. W.B.C., 5,000 per c.mm. (neutrophil polymorphs 57%, lymphocytes 29.5%, monocytes 8.5%, eosinophils 4%, basophils 1%). Bleeding, clotting, and prothrombin times were normal. E.S.R. (Westergren), 18 mm. in one hour. Bone-marrow examination, normal. Serum calcium, 9.7 mg./100 ml.; serum phosphorus, 2.86 mg./100 ml.; plasma phosphatase, 16 units (Bodansky). Total protein, 7.50 g.% (albumin 4.90 g., globulin 2.60 g.). Total cholesterol, 134 mg./100 ml. Plasma alkali reserve, 44 vols.%. Blood urea, 28.8 mg./100 ml. W.R. negative. Moro, Pirquet, and Mantoux reactions (1/10,000 to 1/100), negative.

Urine occasionally showed traces of protein. A water concentration and dilution test was normal (S.G. 1026 to 1000). Porphyrin investigations are reported below.

Liver Function Tests.—Takata–Ara and cadmium, normal; Weltmann, 0.35% $CaCl_2$ (normal, 0.4–0.5); serum bilirubin, 0.83 mg./100 ml. A fat balance was not done.

Progress

The patient was treated with large doses of vitamin D orally and B_2 (riboflavine) orally or intravenously. During the period September 22 to December 24 (94 days) he received a total of 1,458,000 I.U. of vitamin D and 4,675 mg. of riboflavine, with additional vitamins A, C, and B complex. The general condition of the child improved. His rickets improved greatly and his mouth and tongue were better. During this period of treatment several serum and urinary determinations were carried out on the patient and on a control of approximately the same age and weight. The serum and urinary riboflavine levels rose from 3.07 and 62.2 μg./100 ml. on September 24 to 97.0 and 4,062 μg./100 ml. respectively on October 30. The initial serum and urinary riboflavine levels were well below those of the control, which were 25–32 and 164–784 μg./100 ml. respectively. He was readmitted for further investigation in September, 1953. In the 15 months since his previous admission he had grown to 114 cm. in height. His measurements were: crown to pubis, 58 cm.; pubis to heel, 56 cm.; arm span 116 cm. He was still slightly bow-legged, but the *x*-ray film of his hands and forearms showed marked improvement of his rickets (Figs. 2 and 3). There was also considerable improvement of the cataract. Marked porphyrin fluorescence was noted in his upper incisor and molar teeth, but not in his lower incisors. There was no fluorescence elsewhere, except in the circumanal region, and this was due to faecal contamination. His blood plasma did not fluoresce in ultra-violet light. His urine and faeces still contained very large amounts of porphyrin (Table I).

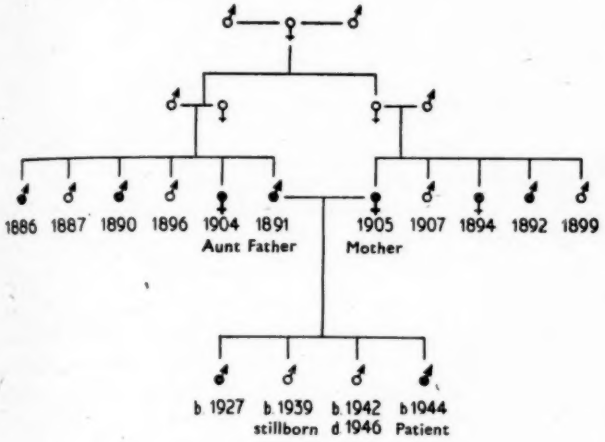
TABLE I.—*Quantitative Determinations. Urinary and Faecal Porphyrins*

	Urine			Faeces		
	Porphobilinogen	Uroporphyrin	Coproporphyrin (μg./l.)	Uroporphyrin	Coproporphyrin (μg./g. Dry Weight)	Protoporphyrin (μg./g. Dry Weight)
Normal (maximal)	Negative	Negative	100	Negative	15	30
Patient ..	,,	Negative*	5,719	,,	2,082	56·8
Mother ..	,,	Negative	500	,,	525	23
Father ..	,,	,,	775	,,	862	44
Aunt ..	,,	,,	295			

* Small amounts detected by chromatographic methods.

Family History

The patient's mother and father are aged 48 and 62 years respectively. Both are healthy and have never had any skin disease, deformity, or growth abnormality. The father is a farmer, and the general diet of the family is undoubtedly satisfactory. The patient has one living brother, aged 26 years, who is normally grown and healthy. Two other brothers are dead. One was stillborn at the sixth month of pregnancy, and the other died at 4 years from pneumonia. The latter was said to have had a brain injury during his birth and suffered from recurrent epilepsy (grand mal). The patient's paternal aunt, aged 59, is alive and well. There is no relevant disease in other relatives, so far as could be ascertained. The family tree is reproduced in Fig. 4.



Family tree. The mothers of the patient's father and mother were stepsisters.
○ Urine and stool not examined.
⊙ Urine only examined. Normal coproporphyrin excretion.
● Increased porphyrin output in stool and urine. (Stool of the aunt not examined.)

FIG. 4

Further Investigations

Porphyrins.—Tables I and II summarize the results of the urinary and faecal porphyrin investigations. There are marked increases in the coproporphyrin III excretion in the four cases. In the mother there is a fivefold and 35-fold increase of urinary and faecal coproporphyrin respectively; in the father an eightfold and 64-fold increase above maximal normal values. The urinary coproporphyrin of the aunt is increased threefold. The urinary and faecal coproporphyrins in the child are particularly high, and are more than 50 and 100 times the maximal normal values respectively. Uroporphyrin I was isolated from his urine in crystalline form as its methyl ester. A porphyrin, which behaved consistently as pentacarboxylic by paper chromatographic methods, was isolated. Although its α band in chloroform and its behaviour both as an ester and as the free porphyrin were distinctive, yet its crystalline appearance and melting-point were very similar to those of coproporphyrin III. Evidence was also obtained by alumina and paper chromatography of the presence of a pentacarboxylic porphyrin in the urine of the mother and aunt, and of a hexacarboxylic porphyrin in the stool of the patient and in the stool and urine of his father.

The urinary amino-acids of the patient and his mother and father, investigated by paper chromatography, showed in each case a "super-glycine pattern." This term is being currently used by Dent (private communication) and his collaborators to describe the pattern shown on a standard urine chromatogram (280 μg. total N) when the amino-acid excretion is comparatively normal except for a large excess of glycine. Those workers have encountered several individuals who appear to excrete amino-acids constantly in this manner. Its pathological significance is still under investigation. Urine from the aunt or other members of the family could not be obtained for this investigation.

The Sulkowitch test in the urines of the patient, mother, and father showed each to have a very high calcium concentration. In the case of the patient the urine was given this test before and after vitamin D treatment had begun.

Discussion

The condition in the four members of the family described above is similar, as regards the disturbances of porphyrin metabolism, to that described by Dobriner (1936) and Watson *et al.* (1949). The pigment excretion in Dobriner's case, in which traces of uroporphyrin were found in the urine along with greatly increased ether-soluble porphyrins, would seem to correspond closely to that of our patient. The demonstration, however, of this abnormal porphyrin excretion as a hereditary trait, less severe in the parents and the paternal aunt, and much more severe in the child, gives the present group of cases a significance which is important. The diseases of porphyrin metabolism have long been described as "inborn errors of metabolism" (Garrod). Congenital porphyria is accepted as being transferred as a Mendelian recessive, while there is strong evidence that acute porphyria occurs as a Mendelian dominant. The inheritance of porphyria cutanea tarda is still in doubt. The condition described above neither clinically nor biochemically corresponds exactly to any of these three diseases. The evidence presented suggests that the genetic pattern of the dyscrasia is heterozygous in the parents and paternal aunt, and is homozygous in the child.

The association of rickets and riboflavine deficiency with excessive porphyrin excretion in our patient is of interest. Rickets has never hitherto been reported in association

TABLE II.—*Chemical Identification of Porphyrins in Urine and Faeces*

		Free Porphyrin		Porphyrin Ester (Paper Chromatography)	M.P. of Crystals (°C.)	Summary
		No. of COOH Groups	α Band in $CHCl_3$ (mμ)			
Patient	Urine	4	621·5	Copro III	140–143, 166–167	Coproporphyrin III
		5	623·0	Between copro I and III	154, 172–178	Pentacarboxylic porphyrin
		8	625·3	Mainly uroporphyrin series I	291	Uroporphyrin I
	Faeces	4	621·3	Copro III	142, 162–166	Coproporphyrin III
		6	623·0			Hexacarboxylic porphyrin
Mother	Urine	4	621·5	Copro III	138–142, 164–168	Coproporphyrin III
		5	622·9			Pentacarboxylic porphyrin
	Faeces	4	621·5	,, ,,	141–143, 164–168	Coproporphyrin III
Father	Urine	4	621·6	,, ,,	143	Coproporphyrin III
		6	622·9			
		4	621·5	,, ,,	140, 164–166	Coproporphyrin III
	Faeces	6	623·3			Hexacarboxylic porphyrin
Aunt	Urine	4				Mainly coproporphyrin
		Trace				(trace pentacarboxylic
		5				porphyrin)

with a porphyrin disorder. The aetiology of the rickets is a matter of question. The bony deformities were noted only at the age of 3½ years. Since the age of 1½ years the mother considered that milk aggravated his skin condition. It is therefore possible that the withholding of milk over a long period contributed to the rickets in a patient whose disease predisposed him to it. On the other hand, renal acidosis or some defect in the renal tubular reabsorptive mechanism, or even steatorrhoea, has not been fully excluded. The fact that the improvement in the bone condition was not accompanied by any marked change in the porphyrin excretion suggests that the association of the rickets and excessive porphyrin excretion is not a close one.

Some relationship may exist between the porphyrin disorder and a predisposition to riboflavine deficiency, since an accidental association of these two excessively rare disorders is most unlikely. It is of interest that Stich (1952) has suggested that riboflavine acts as a regulator of biological porphyrin synthesis, directing it to the formation of the series III porphyrin isomers rather than series I, which, he claims, accumulate excessively when this vitamin is deficient. He based this hypothesis on experimental studies with yeast cultures and supported it with apparently successful therapeutic trials of riboflavine in cases of porphyria. This form of therapy had also previously been advocated by Vannotti (1937), and has also been used by Weingarten (1950) and Lups and Van Dijk (1950). The evidence obtained so far in the present case does not lend support to Stich's hypothesis, since most of the excessive porphyrin excreted is of the III series and only a small amount is excreted as uroporphyrin I. Since the completion of the present studies Antener and Berger (1955) have found that after the administration of 60 mg. of riboflavine daily to our patient, and after periods without riboflavine, the urinary excretions of porphyrin and riboflavine showed an inverse relationship. Thus high levels of urinary porphyrin excretion were associated with low levels of riboflavine excretion, and vice versa. The interpretation of these findings and their possible relation to Stich's hypothesis will be discussed by these authors.

The absence of symptoms, such as abdominal colic or constipation, in every case supports the findings of Goldberg, Paton, and Thompson (1954), that the known porphyrins have no pharmacological action. Our patient has shown no sign of photosensitivity, despite a high daily excretion of coproporphyrin. It has been suggested (Fischer and Zerweck, 1924) that the phototoxic action of the porphyrins is directly proportional to the number of carboxyl groups in the porphyrin molecule; thus coproporphyrin, the main excretion product in this case, would be less active in this respect than uroporphyrin, which is excreted in congenital porphyria and generally in porphyria cutanea tarda. The absence of plasma fluorescence would also suggest a very rapid clearance of coproporphyrin from the circulation, which would prevent an effective concentration of photosensitizing porphyrin in the skin. Watson *et al.* (1949) failed to find raised blood porphyrin levels in their cases. Both these factors—the presence of coproporphyrin rather than uroporphyrin and the efficient elimination of the porphyrin mainly by the faeces—might explain the lack of photosensitization.

The mechanism of the excessive porphyrin production is of interest. In the present case the absence of anaemia, despite the loss of approximately 50 mg. of coproporphyrin daily for several years, would suggest an overproduction of these pigments (Goldberg and Rimington, 1955). The porphyrin is greatly overproduced in the homozygote (the boy), only moderately so in the heterozygotes. This quantitative regulation of the pigments is thus apparently controlled genetically. The main route of excretion of the excess coproporphyrin is via the faeces, which renders unlikely any "renal leak" mechanism. The site of production of these excess pigments is probably the liver or the bone marrow, since one or other of these tissues contains large quantities of porphyrins in the main porphyria diseases. Further work is required to clarify this point. Hoffbauer, Watson, and Schwartz (1953) found that coproporphyrin III, given orally to the rat, was not absorbed from the gut. If this finding is applicable to the human it would make unlikely any theory of gut synthesis of coproporphyrin in this condition. No trial with chlortetracycline has been made so far.

Summary

Four cases of coproporphyria have been described in a single family—a boy aged 10, his mother and father (first cousins), and his paternal aunt. The symptoms of porphyria, such as photosensitivity, abdominal colic, constipation, and paralysis, were absent. The adults excreted moderately high quantities of coproporphyrin III in the urine and stool, whereas the boy excreted very large quantities of coproporphyrin III in the urine and stool, with a trace of uroporphyrin I in the urine. Intermediate porphyrins were also identified—a pentacarboxylic porphyrin in some urines and a hexacarboxylic porphyrin in some stools. In all cases examined the main route of porphyrin excretion was via the stool. The genetic significance of this hereditary porphyrin disorder has been discussed.

The boy also suffered from rickets and riboflavine deficiency, both of which were improved by treatment.

Both the boy and his parents had an amino-aciduria of somewhat unusual character, which is discussed.

The significance of the symptomless nature of this condition and the mechanism of its production are considered.

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REFERENCES

Antener, I., and Berger, H. (1955). In preparation.
Dent, C. E. (1951). In *Recent Advances in Clinical Pathology*, 2nd ed., edited by S. C. Dyke. Churchill, London.
Dobriner, K. (1936). *Proc. Soc. exp. Biol. (N.Y.)*, **35**, 175.
Fischer, H., and Zerweck, W. (1924). *Hoppe-Seyl. Z. physiol. Chem.*, **137**, 176.
Goldberg, A. (1954). *Biochem. J.*, **57**, 55.
—— Paton, W. D. M., and Thompson, J. W. (1954). *Brit. J. Pharmacol.*, **9**, 91.
—— and Rimington, C. (1955). *Proc. roy. Soc. B.*, **143**, 257.
Hoffbauer, F. W., Watson, C. J., and Schwartz, S. (1953). *Proc. Soc. exp. Biol. (N.Y.)*, **83**, 238.
Lups, S., and van Dijk, C. P. (1950). *Ned. T. Geneesk.*, **94**, 1720.
Stich, W. (1952). *Münch. med. Wschr.*, **94**, 842.
Vannotti, A. (1937). *Porphyrine und Porphyrinkrankheiten*, p. 261 et seq. Springer, Berlin.
Watson, C. J., Schwartz, S., Schulze, W., Jacobson, L. O., and Zagaria, R. (1949). *J. clin. Invest.*, **28**, 465.
Weingarten, K. (1950). *Wien. klin. Wschr.*, **62**, 575.

The first issue of a new journal, *Acta Rheumatologica Scandinavica*, has just been published in Stockholm under the direction of an editorial team led by Dr. G. Edström, of Lund. It is the official organ of the Scandinavian Society for Rheumatology, will appear four times a year, and will publish papers in English, French, or German, with summaries in all three languages. Subscription rate is 72s. per annum, and the publisher's address is Drottninggatan 6, Stockholm C.

THE INHERITANCE OF PORPHYRIA

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The porphyrias are disorders involving profound disturbances in the metabolism of pyrrole pigments resulting at times in marked increase in the excretion of porphyrins in the urine. Familial porphyria is associated with cutaneous, psychological, and neurological symptoms. In the quiescent stage either there are no symptoms at all or there is a slightly increased sensitivity of the skin. If the skin is much exposed to the sun the sensitivity becomes more marked. Certain drugs, particularly barbiturates, precipitate an acute attack in susceptible subjects, characterized by abdominal pain, vomiting, and hysteria. Often an acute abdominal emergency is diagnosed and the patient is operated on. When the acute attack has lasted a few days the patient develops a peripheral neuritis which may cause total paralysis. Many of these patients die. During an attack of acute porphyria the urine contains a great excess of porphobilinogen and porphobilin, the latter being mainly responsible for its reddish brown colour.

Historical

It is now 75 years since the first porphyrin was discovered, by treating blood with strong sulphuric acid. The spectroscopic characteristics of the new pigment were described. At about the same time pigment with similar spectroscopic characteristics was detected in the urine of patients with some of the symptoms mentioned above. By the turn of the century a number of cases, widely scattered in Western Europe, had been described in which the urinary excretion of "haematoporphyrin" was greatly increased, and it had also been shown that a slight increase in porphyrin excretion could be detected in the urine of patients with a variety of diseases.

By 1925 the chemists had discovered that several distinct porphyrins occurred in nature, whereas haematoporphyrin prepared as described above was regarded as an artificial pigment not found in natural material. Of particular interest in connexion with clinical cases were uroporphyrin and coproporphyrin, excreted in excess in the urine and faeces of patients suffering from porphyria. It was also shown that each of these porphyrins could theoretically exist in isomeric types I, II, III, and IV, of which only I and III were found in nature. The type III porphyrins possess the same molecular structure as the porphyrin derived from haemoglobin and could not arise from, or be converted into, type I pigments without disruption of the molecule. During the same period the diseases were classified clinically into "congenital porphyria," "chronic porphyria," and "acute porphyria."

During the next 25 years increasing numbers of cases of porphyria were discovered, and improved methods for measuring and identifying the porphyrins were elaborated. At one time it was believed that the different forms of porphyria could be associated with the excretion of different kinds of porphyrin—for example, type I porphyrins in the congenital and type III in the acute forms. Whilst current methods indicate that a preponderance of the relative type excretion exists, the differentiation is not absolute, and paper chromatography has disclosed the excretion of smaller quantities of other porphyrins.

It is now recognized that porphyria is widely distributed, and as interest in, and awareness of, this condition increased, reports of cases became more frequent. Acute porphyria is common in Sweden, where Waldenström (1937) and Waldenström and Vahlquist (1944) have described close on 200 cases. It is also a common disorder in South Africa, where Barnes (1951) has already detailed the case histories and clinical findings in over 40 cases, since when many more isolated cases have been detected, and Dean (1953) has described the personal and family histories of 12 cases of acute porphyria that he has attended. The first three of these patients died, the last nine recovered. Nine further cases of acute porphyria seen since by Dean have all recovered.

A familial tendency in porphyria has been reported previously. Waldenström (1937) encountered several families in Sweden in which more than one case had occurred, and discussed the inheritance at some length. He pointed to three difficulties in securing complete family histories: (*a*) affected persons were seldom aware of medical conditions in their relatives; (*b*) the disease was little known to doctors and was usually misdiagnosed; and (*c*) some susceptible members might not have developed recognizable symptoms at the time of inquiry. Waldenström thought a simple Mendelian dominance was the probable mode of inheritance. He did not find skin lesions, but this may have been owing to the fact that Sweden does not have the year-round sunshine that we have in South Africa.

The classification of porphyria into clinical forms in the past proved most obscure. The problem is the relationship of the intermediate "cutanea tarda" form to the congenital on the one hand and to the acute on the other. Watson (1952) separates the adult "cutanea tarda" and acute types, which he regards as hepatic in origin, from the congenital type starting early in childhood with staining of bone, anaemia, and a large spleen; this type he considers erythropoietic in origin. No cases in the families described here could be regarded as belonging to the rare congenital type, which would appear to be a different entity. Cockayne (1933) discussed the genetics of congenital porphyria as determined from a number of cases in Europe and Japan, abstracted from the literature, and concluded that this form is a recessive disorder due to a single gene, but there is an unexplained partial limitation to the male sex.

The purpose of this paper is to show that porphyria, as it occurs in Europeans in South Africa, is inherited as a Mendelian dominant and that it is not sex-linked. It will also be shown that in these families acute porphyria, chronic cutaneous porphyria, and "symptomless" porphyria are different manifestations of the same inherited disorder. Porphyria as seen in South Africa usually causes no symptoms in childhood.

The Present Study

The genealogies of 13 porphyric families, all of old Burgher stock and almost certainly related far back in South African history, have been traced and a number of other families await investigation. A total of 236

members (121 male and 115 female) had clinical manifestations of porphyria. Many of them had sensitive skins that abraded easily and occasionally blistered. The sensitivity is most marked on the back of the hands and the face. The water blisters, when they occur, are small, usually about half an inch (1.3 cm.) in diameter, the blister breaks and leaves a sore, and eventually the hands may be scarred from many healed lesions. In some individuals the skin sensitivity is very slight and occasional. If cutaneous manifestations are present porphyrins can be detected in the urine by spectroscopic examination and by fluorescence in ultra-violet light, even though the urine may appear normal in colour. If no obvious skin sensitivity is present there may be a very little increase in the excretion of porphyrin in the urine.

Despite having a sensitive skin, most male porphyrics feel well throughout life and never develop an attack of acute porphyria. However, if they are given a thiopentone anaesthetic or take an excess of barbiturates an attack of acute porphyria may result. In women the cutaneous manifestations are usually slight, although often more apparent during pregnancy. However, in South Africa they generally know that their exposed skin is more sensitive than average and an occasional blister may have appeared. The increased sensitivity of the skin in men may be due to the fact that men are more consistently exposed to the sun and to trauma. The full explanation of the differing manifestations in the sexes is not understood; endocrine factors may be involved.

Porphyrics, particularly women, often appear to be emotionally unstable; they complain of abdominal pains for which no cause can be found, and are often given barbiturates to relieve their symptoms, which become worse. They may persuade a surgeon to open the abdomen in the hope of finding some gynaecological or other cause for their pains. If porphyria is not diagnosed, and it seldom is, an acute attack of porphyria is very likely to occur in female porphyrics at some time during their lives. The attack is nearly always precipitated by drugs, especially barbiturates. In the acute attack the abdominal pains become severe, there is marked emotional disturbance, and over the course of a few days a generalized paralysis due to peripheral neuritis occurs. A great excess of porphyrins and porphobilinogen can then be found in the urine, which is reddish brown in colour. These attacks are associated with a marked disturbance of liver function.

Although 13 family groups have been investigated only one will be presented in this paper (see genealogical tree). We have been singularly fortunate in being able to carry out a complete survey of the urines of the living members. All the families follow a similar pattern so far as we have been able to study them.

The founder of the family described came to South Africa from Holland in 1713; his wife's family came in 1688. His great-grandson, who was born in 1788, had four sons and one daughter, and many of the descendants of three of his sons are porphyrics. The third son, born in 1814, has had 478 descendants, 434 of whom are still alive; all of them have been traced. To-day there are members of this branch of the family in Germany, France, England, the United States, and the Rhodesias. They have all been contacted, their histories obtained, and their urine examined for porphyrin. Rimington (1952) and Wells and Rimington (1953) have emphasized the importance of estimating the faecal porphyrins. This has already been done in a number of members of this family, and a fuller account will be published in due course. In two cases a suspected parent's urine was repeatedly negative for porphyrins, although one or more descendants were undoubtedly positive; their faecal porphyrins, however, were high.

Collection and Examination of Urine

Many of the surviving members of the family still live in the Alexandria district of the Cape Province; some have migrated to other districts and more widely to the other three provinces. A few were followed to addresses overseas. In this investigation one of us (G. D.) traced the various members, to whom letters were sent explaining the circumstances, inviting their co-operation by giving information and by submitting one or more specimens of urine. This involved a great deal of correspondence and much exasperation, but the eventual response was exceptionally good. Wherever possible information was also obtained from doctors attending the members. The urine specimens, preserved with chloroform, were sent to one of us (H. D. B.), who was not informed at the time of the family group from which the specimens came.

The urine was almost invariably turbid when received for examination and was filtered after the addition of a little "celite" (Johns Manville Co.); with a few exceptions the filtrates were quite clear, so that a deep layer up to 4–5 in. (10–12.5 cm.) of the paler specimens could be examined with a spectroscope against a good light. Thinner layers of more coloured specimens were examined so as to provide the best conditions for detecting any bands present in the green portion of the spectrum. About one-tenth volume of concentrated hydrochloric acid was then added to the filtered urine and spectroscopic examination repeated. Observation of two bands at about 540 and 580 mμ, which in the acidified specimen were replaced by a slightly broader band at 555 mμ, was regarded as indicating the presence of porphyrin. Examination of untreated and acidified urine in ultra-violet light for the characteristic orange or red fluorescence was always used as a check, but this method was less sensitive than spectroscopic examination.

Most of the specimens recorded as positive gave unequivocal results, but in a survey such as this it could be expected that some of the positive members were likely to be tested during a clinically quiescent stage of the disorder. With a few specimens the bands were so faint that the observer was left in some doubt of their actual presence, and repeat specimens were obtained which usually helped to clear the distinction between positive and negative findings. The requirement that the spectra of both metal complex and acid porphyrin should be seen in the appropriate specimens was a safeguard against reporting a trace of blood as porphyrin. If any doubt existed on this point it was resolved by use of the pyridine haemochromogen test. In a few specimens the pink colour of urorosein formed on acidification. These were recognized by the absorption band in the green being broader than that of acid porphyrin, and also by their negative fluorescence in ultra-violet light. Examination of the faeces for increased porphyrin excretion is of the greatest value when the diagnosis is in doubt. In young children particularly, the urine excretion was always normal, although a number must have inherited porphyria. A survey of the faecal porphyrin excretion in their cases is being undertaken.

The Inheritance

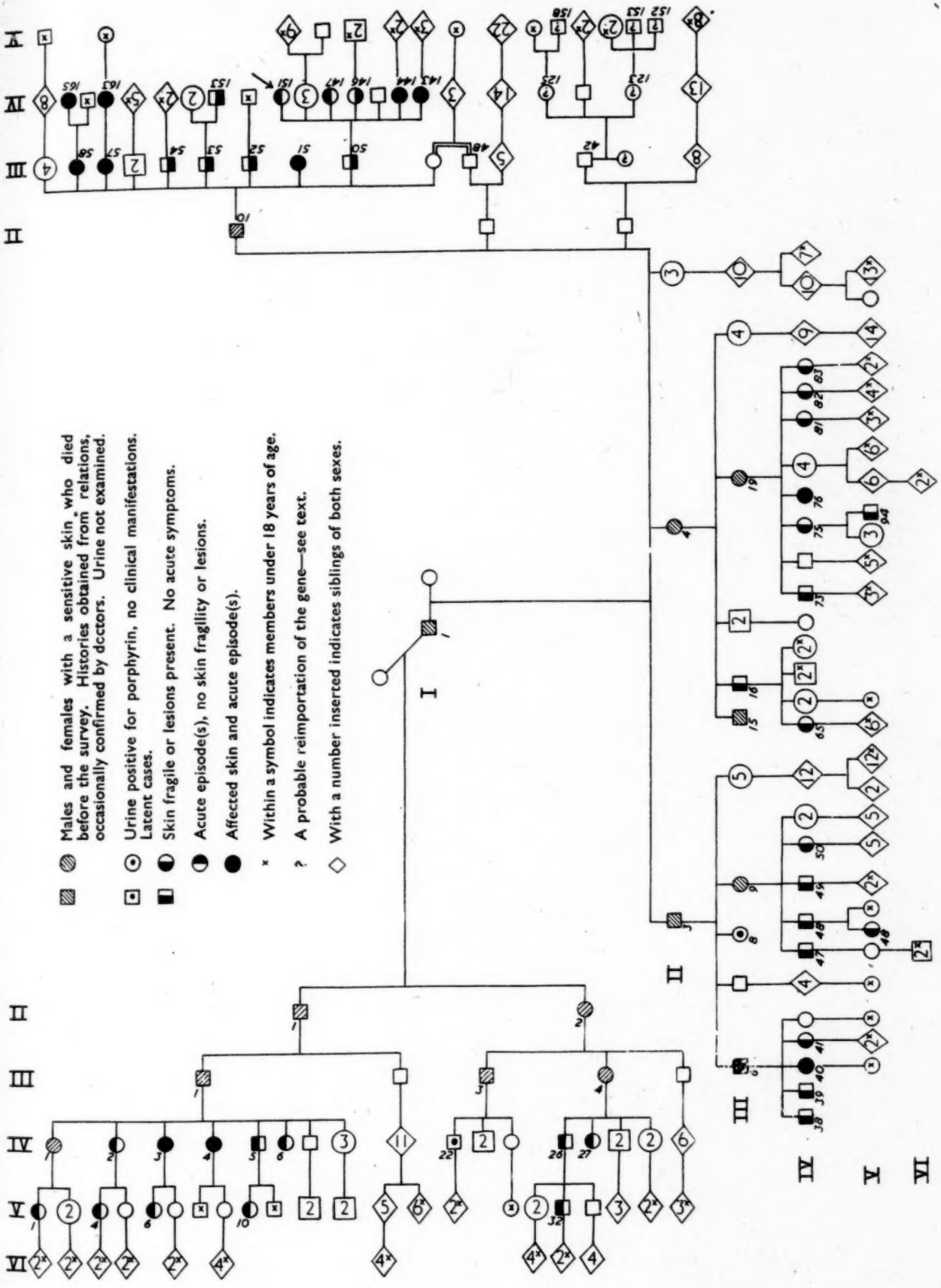
According to Mendelian law, if a dominant characteristic is present in one partner only, half the descendants should inherit the dominant characteristic.

There are 60 porphyrics among the 125 descendants with a porphyric parent in the group shown in Table I, excluding

TABLE I.—*Number of Members in Each Generation, Total Adult Children of Affected Parents, Number and Percentage of Affected Children. The Members in the Family with the Reimported Gene are Not Counted.*

Generation	Total Members	Adult Children of Affected Parent			Affected			% Affected
		No.	M	F	No.	M	F	
I	1							
II	10	10	5	5	5	3	2	50
III	62	37	16	21	16	9	7	43·2
IV	173	59	17	42	32	10	22	54·2
V	201	19	3	16	7	2	5	36·8
VI	32	—	—	—	—	—	—	—
Total	479	125	41	84	60	24	36	48

Generation V contains many juveniles and young adults, some of whom may yet show symptoms and raise the percentage of affected persons. All the members of generation VI are under 18 years of age.


Males and females with a sensitive skin who died before the survey. Histories obtained from relations, occasionally confirmed by doctors. Urine not examined.
Urine positive for porphyrin, no clinical manifestations. Latent cases.
Skin fragile or lesions present. No acute symptoms.
Acute episode(s), no skin fragility or lesions.
Affected skin and acute episode(s).
Within a symbol indicates members under 18 years of age.
A probable reimportation of the gene—see text.
With a number inserted indicates siblings of both sexes.
I
II
III
IV
V
VI

those under the age of 18 years. In all cases only one parent is a porphyric. Five of the 10 children in the second generation are porphyrics. In the third generation there are 16 porphyrics among the 37 children with a porphyric parent. In the fourth generation there are 32 porphyrics among the 59 children with a porphyric parent. In the fifth generation there are seven known porphyrics among the 19 descendants with a porphyric parent, all young but over the age of 18 years. In this family 48% of the adults with one porphyric parent inherited porphyria; 24 out of the 41 male descendants with an affected parent, and 36 out of 84 female descendants. The corresponding figures for all 13 families together were 53.4%; 51.3 M.: 48.7 F. These conform with the theoretical requirements of a non-sex-linked Mendelian dominant type of inheritance.

The progenitor of the family group described in detail can be remembered by one remaining son-in-law, now naturally a very old man. The progenitor of this group suffered from blisters and sores on his hands much of his life. Five members (IV 123 and 125, V 152, 153, and 158) have consistently given laboratory results which, for the time being, must be regarded as equivocal. These are descendants of III 42; there is no evidence that he or his father (both deceased) were affected, but his wife is stated to have a sensitive skin and has shown traces of porphyrin in three specimens of urine. This group is being further studied, but is excluded from the count in Table I since, even if the affection is confirmed, it cannot be regarded as inherited from the progenitor, but has been acquired by reimportation. All the other affected members of the family have descended from the five affected children of the progenitor. This man had three brothers and one sister; many of the descendants of two of his brothers and two of his cousins are also porphyrics. In a subsequent paper it is anticipated that it will be possible to show that all Afrikaner porphyric families stem from a common forebear. In the family described there are 10 children, 62 grandchildren, 173 in the fourth generation, 201 in the fifth, and already 32 in the sixth. Of the descendants over the age of 18 years, 60 have inherited porphyria.

Only 4 of the 36 women (Table I) who inherited porphyria had severe skin sensitivity. In the remainder the skin sensitivity was very slight. Including the progenitor, 61 adults in the family have inherited porphyria (25 male and 36 female), 39 are still alive and porphyrins have been found in the urine of 35 of them; one urine is doubtful and three are negative. Among the 22 who died (8 male and 14 female), 1 man and 8 women have died with typical symptoms of acute porphyria.

Twenty-five men in this group have inherited porphyria, of whom 17 are still alive. Sixteen of the 17 have sensitive skins and multiple scars on their hands from previous blisters and sores. Most of them are free of symptoms except for the skin sensitivity and do not take drugs. Acute porphyria and abdominal symptoms are comparatively uncommon in male porphyrics, and most of them die eventually from some other cause. If they have been warned of the dangers of taking certain drugs, including excess alcohol, the danger of acute porphyria would appear to be slight.

Thirty-six women have inherited porphyria in this group, and 22 of them are still alive. Eight have died from acute porphyria; a further five have had attacks of acute porphyria and have recovered. Most of the women suffer from periodic attacks of abdominal pain. A similar high proportion of acute attacks in females was found in the other families investigated. Unless the condition is correctly diagnosed in a woman, and she is warned of the dangers of taking certain drugs, it is likely that sooner or later she will have an attack of acute porphyria. Porphyrics should be given a letter showing the evidence that they suffer from the disorder and emphasizing the danger of taking certain drugs. They should be asked to show the letter to any doctor who attends them or their children.

Eleven cases of acute porphyria in the group are described in detail.

Case Reports

III 6.—A man, died aged 46, Johannesburg (1932). The history was obtained from his wife and from the hospital records. He had suffered from a sensitive skin that blistered easily since he was 20 years old. At the age of 30, after taking sleeping tablets, he had an attack of severe abdominal pain. His abdomen was opened but no pathological condition was found. He continued to take sedatives and had recurrent attacks of abdominal pain until his final illness. During the last year of his life the pains increased in severity, and he lost 80 lb. (36.3 kg.) in weight; he was very

TABLE II.—*Summary of Positive Cases Giving Clinical Status, the Urine Findings, and the Source of the Information. The Member is Indicated by Generation (Roman Figure) and Serial Number (Arabic Numeral) Corresponding to the Chart*

Member	Sex	Skin	Acute Symptoms	Urine	Comment
I 1	M	++	None		Deceased
II 1	M	++	,,		,,
II 2	F	+	,,		,,
II 3	M	++	,,		,,
II 4	F	+	,,		,,
II 10	M	++	,,		,,
III 1	M	++	,,		,,
III 3	M	++	Mild psy. and neurol.		,,
III 4	F	+	None		,,
III 6	M	++	+ Fatal	Dark	History below
III 8	F	Neg.	None	+	Seen G. D.
III 9	F	+	,,		Died, heart disease
III 15	M	++	,,		Deceased, seen family doctor
III 16	M	++	,,	Neg.	Quiescent, seen G. D. Faecal porph.+
III 19	F	+	,,		Deceased
III 50	M	++	,,	+	Seen G. D.
III 51	F	++	+ Fatal	+	History below
III 52	M	++	None	+	Seen G. D.
III 53	M	++	,,	+	,, ,,
III 54	M	++	,,	+	,, ,,
III 57	F	+	+ Recovered	+	Report from own doctor
III 58	F	+	+ ,,	+	History below
IV 1	F	+	None		Deceased
IV 2	F	Slight	Slight abd. pain	+	Quiescent, seen H. D. B.
IV 3	F	++	+ Fatal	Red	History below
IV 4	F	++	+ ,,	+	,, ,,
IV 5	M	++	None	+	Quiescent, seen H.D.B.
IV 6	F	+	Abd. pain	Neg.	Report from own doctor
IV 22	M	Neg.	None	+	Seen G. D.
IV 26	M	Slight	,,	Neg.	Seen G. D. Faeces?
IV 27	F	+	,,	?	
IV 38	M	++	,,	+	Seen H. D. B.
IV 39	M	++	,,	+	,, ,,
IV 40	F	++	+ Recovered	+	Seen G. D.
IV 41	F	+	Occ. pain	+	Report from own doctor
IV 47	M	++	None	+	Seen G. D.
IV 48	M	++	,,	+	,, ,,
IV 49	M	++	,,	+	,, ,,
IV 50	F	+	Occ. pain	+	,, ,,
IV 65	F	+	None	+	,, ,,
IV 73	M	++	,,	+	,, ,,
IV 75	F	+	,,	+	Report from own doctor
IV 76	F	+	+ Fatal	Red	History below
IV 81	F	+	None	+	Report from own doctor
IV 82	F	+	Occ. pain	+	,, ,,
IV 83	F	+	None	+	Seen G. D.
IV 143	F	+	+ Recovered	+	Report from own doctor
IV 144	F	+	+ Fatal	Dark	History below
IV 146	F	+	Occ. pain	+	Seen G. D.
IV 147	F	Neg.	+ Fatal	Red	History below
IV 151	F	Slight	+ ,,	+	,, ,,
IV 153	M	++	None	+	
IV 163	F	+	+ Fatal	Port wine	History below
IV 165	F	+	+ Recovered	+	,, ,,
V 1	F	+	Occ. pain	+	Seen H. D. B.
V 4	F	+	,, ,,	+	,, ,,
V 6	F	+	None	+	Seen G. D.
V 10	F	+	,,	+	Seen H. D. B.
V 32	M	++	,,	+	,, ,,
V 48	F	+	,,	+	Seen G. D.
V 94	M	++	,,	+	Report from own doctor

Skin + indicates slight sensitivity; perhaps only an occasional blister or exposed skin abrades when scraped with the thumb nail.

Skin ++ indicates marked sensitivity present or past. Most of the survivors have been seen personally by one of us. The histories of deceased members were obtained from doctors or relatives.

constipated. Finally, he became delirious, and on admission to hospital had to be manacled. He was given repeated injections of morphine and hyoscine. His urine was of port-wine colour. He was thought to have an intestinal obstruction, and a barium meal examination showed apparent delay in the small bowel. He was given a bromethol rectal injection so that a laparotomy could be performed, but his condition became so grave that the abdomen was not opened. He died a few hours later without regaining consciousness. Permission was not given for a necropsy, and death was certified as due to "chronic obstruction of ileum." Four of his five children have inherited porphyria.

III 51.—A married woman, died aged 57, Bloemfontein (1949). Information was obtained from the doctor who attended her. She had suffered periodically throughout her adult life from attacks of abdominal pain and had consulted many doctors. Her skin did not blister, but it was unduly sensitive. She had always been of a nervous and rather hysterical disposition, and had been told by most of her advisers that her symptoms were due to her nervous state. Sedatives, usually barbiturates, had been prescribed for her. A few months before her death her symptoms became more pronounced; she was very constipated and lost over 40 lb. (18 kg.) in weight. A month before her death she complained of marked weakness in her arms and legs and was admitted to hospital. While in hospital it was noticed that her urine was "port wine in colour." No bilharzia ova were found and only an occasional red corpuscle. The blood count, blood urea, and cerebrospinal fluid were normal. Ten days after admission to hospital her urine was tested chemically and spectroscopically for porphyrins; the tests were positive. The urine was sent to the Institute for Medical Research in Johannesburg, where the porphyrinuria was confirmed. By this time she had become paralysed, the blood urea rose to 173 mg. per 100 ml., and she died. Permission was not granted for a necropsy.

III 58.—Morgenzon, Transvaal (1953). This woman is alive, but a detailed history is given because of its interest. She had been traced in the investigation of the family tree, but no excess of porphyrin could be detected in her urine; however, her daughter had porphyrinuria (IV 165). She had been warned in writing that she had almost certainly inherited porphyria, and she had been informed of the type of symptoms she might suffer, in particular abdominal pains. She had been advised to warn her doctor that she could not take certain drugs, particularly barbiturates and especially a thiopentone anaesthetic. As she could not be interviewed personally, she was requested to show her doctor the letter. Despite these precautions, she allowed her doctor to give her a thiopentone anaesthetic in order to carry out an operation without informing him she was a porphyric. After the operation her condition deteriorated and she passed a dark amber urine. She gradually became paralysed. Only at this stage was a consultant, who had been called in consultation, shown the warning letter. Her urine was strongly positive when tested for porphyrins. All drugs were stopped and she was fed intravenously. She slowly recovered, and now, many months later, she is able to walk and has left hospital.

IV 3.—A woman, died aged 40, Capetown (1953). This member of the family was traced only with great difficulty. A letter was sent to the patient warning her that she might be a porphyric, describing the symptoms and explaining the danger of taking certain drugs, particularly barbiturates. Three days later a reply was received from her daughter, who described how her mother had suffered from a sensitive skin and attacks of abdominal pains for many years; how a week before the arrival of the letter she had started to take 6 gr. (0.4 g.) of pentobarbitone sodium at night. The pains had increased, she became delirious and passed a reddish-brown urine. Her urine was found to contain a great excess of porphyrins. A second letter a few days later related how she had become paralysed and died. The letter warning her that she might be a porphyric had arrived a few days too late. The history was confirmed by the family doctor.

IV 4.—A woman, died aged 33 in France (1928). The husband of this woman was last heard of in 1928, at the time of his wife's death. He was thought to be somewhere in France, but his address was unknown. All that was known about him was that he originally came from Cardiff. A letter was sent to the Lord Mayor of Cardiff explaining the necessity of tracing the husband, as his children might have inherited porphyria. With the assistance of the Cardiff police he was traced to his present address in France. The husband described how his wife had suffered from a skin that blistered easily, particularly on the face and hands. She also developed small areas of pigmented skin on the face. Her ankles tended to swell, and she often suffered attacks of severe abdominal pain. After taking certain drugs at the beginning of her third pregnancy she developed severe abdominal pains, became delirious, and passed a red urine. Over the course of a few days she became paralysed and died. Death was certified as due to "black-water fever."

IV 76.—An unmarried woman, died aged 33, Port Elizabeth (1933). She had had a sensitive skin since she was 18. She used often to suffer from attacks of abdominal pains and took a great deal of drugs, particularly for her "nerves." Following a week of severe abdominal pain she was admitted to hospital, where appendicitis was diagnosed. Bromethol was given and her appendix was removed. Even before the operation it was noticed that her urine was red in colour. After the operation she was very hysterical and was heavily sedated. Over the course of a week she became almost totally paralysed and her knee- and ankle-jerk reflexes disappeared. She died three weeks after the operation.

IV 144.—A woman, died aged 27, Grahamstown (1942). She was admitted to hospital because of severe abdominal pains, loss of weight, and marked weakness in the arms and legs. She was very hysterical and was heavily sedated with barbiturates and morphine. While in hospital it was noted that her urine was "deep amber" in colour. Within a few days her arms and legs were paralysed and a fortnight after admission to hospital she died. The family remember that she had a sensitive skin that blistered occasionally.

IV 147.—An unmarried woman, died aged 22, Port Elizabeth (1942). So far as the family remember, her skin was not noticeably sensitive. Her final illness started with abdominal pains and she became very constipated and vomited frequently. Over the course of a few weeks she lost a great deal of weight. She was given sedatives; her symptoms became so severe that she was admitted to hospital and given repeated injections of morphine for pain. At this stage she was passing a red urine, but no blood was present. A few days after admission her arms and legs were paralysed, and she died on her seventeenth day in hospital. Death was certified as due to myelitis and pyelonephritis. No further records are available.

IV 151.—A nurse, died aged 19, Uitenhage (1951). Her skin was slightly sensitive, but did not blister. She had always been of a nervous disposition and often suffered from pains in her jaw, abdomen, and limbs. She treated herself with drugs that she obtained from the hospital. Two months before her death she had all her teeth extracted because of pains. After this her symptoms became worse and she took larger doses of analgesic and sedative drugs. She complained of severe abdominal pains, vomited frequently, and was extremely constipated. As she was thought to have an intestinal obstruction a laparotomy was performed, but no obstruction was found. Thiopentone was used as an anaesthetic. After the operation she was delirious, vomited repeatedly, and had great abdominal pain. Within three days she became almost completely paralysed, her pulse was rapid, and her pupils were dilated. All the reflex jerk responses were absent. Her urine was dark amber in colour and when it was examined porphyrins and porphobilinogen were found in great excess. The urine fluoresced in ultraviolet light, and spectroscopic examination showed the porphyrin absorption bands. At this stage she was being fed intravenously. Although all drugs were stopped as soon as the diagnosis of acute porphyria was made, she died within

a week of the operation. G. D. was called in consultation to see this case. She was the propositus of this genealogical study.

IV 163.—A married woman, died aged 24, Durban (1950). For three years before her death she had complained greatly of abdominal pains. On two occasions she was treated as a case of pyelitis because she passed a red-coloured urine. An abortion occurred in 1947, and five months before her death she gave birth to a live child. During and after pregnancy she suffered from severe attacks of abdominal pain; she frequently vomited and was very constipated. She lost a great deal of weight. She was in a very nervous state and was taking barbiturate sedatives. Six weeks before her death it was noticed that her urine was "port wine in colour." As her symptoms were becoming worse she was admitted to hospital, where a generalized paralysis of lower motor neurone type developed. She was treated with deoxycortone acetate and ascorbic acid. After a week of almost complete paralysis she died. The details about her history were obtained from her mother and the family doctor.

IV 165.—A married woman, aged 24, acute porphyria (1954). During her 20th year she suffered from extreme nausea early in her first pregnancy, but continued to full term and gave birth to a live child. Two years later she was treated for lower abdominal pain and the cervix was cauterized. Eight months later there was an episode of epigastric pain with vomiting. Although her mother's (III 58) urine was negative when first tested for porphyrin, her urine contained an excess of porphyrin and she was warned in writing that she was a porphyric. The danger of drugs was emphasized. Seven months after this, believing herself again pregnant, she took certain drugs. She developed extreme nausea and vomiting, with abdominal pain. Constipation was marked. She became acutely ill and was fed intravenously. Her urine was reddish brown in colour, and when examined contained a great excess of porphyrin and porphobilinogen. At this stage her skin was very sensitive and abraded very easily. There was weakness of her limbs, but no true paralysis. The symptoms slowly subsided and she was discharged from hospital after three weeks.

Summary

The family tree from a large porphyric family group is presented. This group is typical of twelve others that have been investigated. In all these groups porphyria has appeared in its acute form, in its chronic cutaneous form (the "cutanea tarda" type), or as a symptomless porphyrinuria. In many cases one type changed into the other. They are different manifestations of the same inherited disorder.

It is shown that 50% of the children of a porphyric parent will inherit porphyria and that the distribution of the inheritance between the sexes is approximately equal. That is, porphyria as it occurs in South Africa is inherited as a Mendelian dominant characteristic and is not sex-linked.

If porphyria is inherited, cutaneous manifestations are more pronounced in men and are often very slight and infrequent in women. On the other hand, acute attacks are common in women. The reason for this is not fully understood. Men are more constantly exposed to the sun and to trauma; women appear more likely to be given sedative drugs or to be operated on for abdominal pain, often under a barbiturate anaesthetic. There may also be endocrine factors.

In the latent stage diagnosis may be difficult. The personal and family history is of the utmost importance, and the urine and faeces should be examined by a biochemist who is experienced in detecting porphyrins.

When a case of porphyria is diagnosed it is important to trace the genealogical tree and to investigate the other members of the family group. These investigations will usually result in the discovery of many other cases who could then be warned of the inherent danger.

We would like to express our appreciation to Mrs. C. van der Walt, who undertook the vast correspondence involved in this research; to Dr. K. van der Walt, who was responsible for the family tree; and to Dr. J. A. Fraser Roberts for advice about the final draft. Our thanks are also due to Dr. F. W. K. Grotepass, of Pretoria University, and all the other doctors in South Africa, Europe, and America who have given us their co-operation.

REFERENCES

Barnes, H. D. (1951). *S. Afr. J. clin. Sci.*, **2**, 117.
Cockayne, E. A. (1933). *Inherited Abnormalities of the Skin and its Appendages*. Oxford Univ. Press, London.
Dean, G. (1953). *British Medical Journal*, **2**, 1291.
Rimington, C. (1952). Second International Congress of Biochemistry. Paris.
Waldenström, J. (1937). *Acta med. scand.*, Suppl. 82.
—— and Vahlquist, B. (1944). Ibid., **117**, 1.
Watson, C. J. (1952). *Diseases of Metabolism*, 3rd ed., edited by G. G. Duncan. Philadelphia.
Wells, G. C., and Rimington, C. (1953). *Brit. J. Derm.*, **65**, 337.

QUININE AMBLYOPIA

TREATMENT BY STELLATE GANGLION BLOCK

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Quinine, which was discovered more than 300 years ago, has proved of inestimable value in the treatment of malaria. It has played a lesser part in the treatment of muscular dystrophies. It has frequently been incorporated in proprietary and home-made antifebrile mixtures and tonic wines. Its use as an abortifacient has been reported on several occasions.

In susceptible people a dose as small as 1 gr. (65 mg.) may produce transient disturbance of vision. Permanent optic atrophy with restricted visual fields has been reported in the case of a man who drank two bottles of proprietary orange-and-quinine wine. By contrast others, especially those living in tropical climates, have taken doses of between 100 and 200 gr. (6.5 and 13 g.) daily without obvious ill effects. There has never been a satisfactory explanation for the wide range of sensitivity to this drug. Unfortunately, the sale of this potentially dangerous substance is unrestricted and the grave risk of permanent damage, especially to the visual apparatus, is insufficiently appreciated.

Case History

A married woman aged 31, knowing herself to be eight weeks pregnant and wishing to procure an abortion, purchased without difficulty ½ oz. (15 g.) of powdered quinine sulphate at a chemist's shop. At 1 a.m. on Sunday, January 2, 1955, she dissolved the powder in a glass of port and drank the contents of the glass. Within a few minutes her vision was blurred and she experienced buzzing in her ears. She went to bed feeling very ill and in about an hour's time began to vomit. The vomiting continued repeatedly, but she eventually fell asleep. At 7 a.m. the same morning she awoke to find herself completely deaf and completely blind. She remained deaf and blind throughout that day, and by the following morning the blindness was still absolute, but the hearing had improved. She was admitted to the Royal Halifax Infirmary at 4 p.m. on January 3.

On admission she was quite rational and was able to give a full account of her activities. She was not sweating, her colour was good, and she was not in any way distressed. The pulse was 90 a minute and regular, respirations 18, and blood pressure 120/80. She was able to hear when addressed in an ordinary conversational tone. The pupils were equal, widely dilated, and fixed. Full ocular movements were retained, but she was completely blind. Extreme pallor of the optic disks and of both retinae was observed. No abnormality of note was discovered in the other systems. An electrocardiogram was normal. When seen by an ophthalmologist at 7 p.m. the complete absence of perception to light was confirmed. He noted extreme pallor of the optic disks with blurring of the edges of the disks. He also commented on the milky appearance of the retinae due to oedema, especially around the maculae. Narrowing of the retinal vessels was most obvious in the smaller branches, and the terminal twigs were invisible.

Treatment

In view of the marked vascular spasm and the observed pallor of the optic nerves and maculae, she was treated with vasodilators and intensive vitamin B intravenously. Papaverine hydrochloride 1 gr. (65 mg.) was given intravenously at once, and this was reinforced by sodium nitrite, 100 mg. intravenously. The papaverine was continued four-hourly but no further sodium nitrite was given.

At 10 p.m. "parentrovite," one pair of ampoules, was injected intravenously and thereafter six-hourly. This preparation consists of massive proportions of the total vitamin B complex together with vitamin C. At 10.30 p.m., when the blindness had been present for at least 39½ hours, and because there was no obvious improvement, bilateral stellate ganglion block was performed.

Numerous techniques are available for this procedure. Success is assured by familiarity with one method. On this occasion a high antero-lateral approach was used under local analgesia. The patient lies in a supine position with the head turned slightly toward the side opposite the one to be blocked, with a pillow under the nape of the neck. A skin weal is raised with 1% procaine two fingerbreadths above the clavicle at the level of the posterior edge of the sterno-mastoid muscle. This point is located a little below the angle formed by this muscle and the external jugular vein. The vein, if not easily seen, can be made to stand out more clearly if the patient is asked to cough whilst the nose is nipped momentarily by an assistant or by the patient himself.

The fingers of the left hand palpate the transverse processes of the cervical spine by depressing the skin in the groove behind the sterno-mastoid muscle. The most prominent bony point is the tubercle of Chassaignac, and below this lies the transverse process of the seventh cervical vertebra. A lumbar puncture needle 8–10 cm. long is inserted through the weal perpendicular to the skin, aiming for the correct sagittal bony plane, and if accurately directed comes to rest at the junction of the transverse process and the body of the seventh cervical vertebra. The ganglion lies slightly below this point, separated from the bone by the longus colli muscle. After careful aspiration, to ensure that neither a blood vessel nor the spinal canal has been accidentally punctured, 10 ml. of 1% procaine is slowly injected.

The right side was done first but without benefit. Within a minute of completing the left stellate ganglion block, and as the ptosis of the left upper lid was appearing, the patient spontaneously exclaimed, "I can see you." At that time, in a darkened ward and with only the illumination of a headlamp, she was able to count fingers with her left eye at one metre and to see faces at the foot of the bed. At this juncture we learned that since childhood she had only been able to perceive light with her right eye, owing to an extensive degree of myopia, and was wholly dependent on her left eye. This accounted for the apparent failure of the right stellate ganglion block. Though complete ptosis of the left upper lid was apparent the left pupil remained fixed and dilated. The initial improvement was not fully maintained, and for this reason bilateral stellate ganglion block was repeated daily. The papaverine and parentrovite were continued, but were reduced to twelve-hourly injections by January 6. All treatment was suspended on January 7, the fifth day of admission. Acid sodium phosphate, 20 gr. (1.3 g.) three times daily, was given in order to facilitate excretion of quinine in the urine.

Progress

There was a notable and immediate improvement in visual acuity after each stellate ganglion block was completed, and by January 7 the patient asserted that the vision in her left eye was as good as it had ever been before, but that everything appeared dark "as though it were 4 o'clock on a winter's day." Appreciation of colour, on the other hand, for the red end of the spectrum returned early and was maintained throughout. Repeated observations of the fundi and of the visual fields were made, and at the final assessment on March 5 it was observed that the disks were still very pale, the retinal vessels still narrowed, but the oedema had disappeared. Corrected visual acuity in the left eye was 6/9. This was the same as it had been before taking the quinine. The visual field in the left eye, which had been considerably reduced, was now greatly improved, though it still showed a slight constriction at the periphery.

On January 18 vaginal examination was performed. The uterus was found to be enlarged, but smaller than expected for the estimated duration of pregnancy. It was suspected that the foetus had perished. On February 4 she passed a large blood clot spontaneously and bleeding continued per vaginam. This determined the need for evacuation of the uterus, and on February 12, under general anaesthesia, the residual products of conception were removed.

Discussion

Our experience in this case has thrown some light on the pathogenesis of quinine amaurosis. The relative roles of direct damage to nerve elements, especially the ganglion cells of the retina, and vascular spasm are still in dispute. Many authorities, including Ballantyne when discussing a case presented by King (1934–5) at the Royal Society of Medicine, have noted the appearance of amaurosis before vascular spasm could be demonstrated. Experimentally, too, in animals, damage to nerve elements has been shown to precede vascular changes. By contrast others have stressed the importance of vascular spasm. Braveman *et al.* (1948), reporting a case of quinine amblyopia, state that "the outstanding finding in the fundi was the markedly persistent vasoconstriction that led to severe retinal damage." Whatever the truth, all authorities are agreed that treatment should be directed towards producing vasodilatation. Intensive vitamin B therapy was tried in our case in addition, partly for its vasodilator effect and partly in the hope that it would reverse, or at least retard, damage to nervous tissue. Atropine, acetylcholine, and amyl nitrite have been recommended. Others, quoted by Duke-Elder (1940), have suggested paracentesis of the anterior chamber or corneo-scleral trephining.

Our own attempts to produce vasodilatation by drug therapy were ineffectual. Stellate ganglion block, on the other hand, was seen to reduce vascular spasm and to initiate an immediate return of central vision. From this it is reasonable to infer that vascular spasm was an important factor in the causation of the blindness, that it could occur early, and that it was reversible irrespective of the concurrent damage to nervous elements in the retina. Furthermore, the repeated clinical observation that the peripheral field of vision is always more seriously and more permanently affected suggests that quinine may have a selective toxic action on the rods, which are more abundant at the periphery. This view is confirmed by the fact that blue vision returned late, whereas red vision was appreciated as soon as the visual acuity improved. It is widely held that the rods are concerned with blue vision.

The capacity of stellate ganglion block to produce dilatation of cerebral vessels has been a further matter for dispute. Naffziger and Adams (1950) reported the use of this manœuvre in a series of 155 patients suffering from acute cerebrovascular accidents together with 70 other cases suffering from a variety of cerebral disorders. Whilst admitting the difficulty of assessing the effectiveness of this measure in a disorder with such a variable response without special treatment, they conclude that their results were sufficiently gratifying to encourage its use in cases in which cerebrovascular spasm could be inferred. Leriche (1952) and Walsh (1954) have strongly advocated stellate ganglion block in the treatment of recent and late cases of cerebral thrombosis. Our experience in this case has shown that sympathetic denervation can effectively dilate the retinal arteries and by inference can dilate other cerebral arteries under control of the stellate ganglion. As a corollary it is suggested that stellate ganglion block might prove of considerable value in the treatment of other forms of retinal vascular constriction, and especially in the treatment of thrombosis of the central retinal vein and of embolism of the central retinal artery. Cotson (1951) reports a case in which stellate ganglion block was done 5½ hours after the onset of sudden blindness due to an embolus of the central retinal artery. Within fifteen minutes there was a marked dilatation of the entire retinal tree and the embolus was seen to pass into the periphery of the fundus. Within a few days vision was restored.

The effect of quinine on the foetus is worthy of comment. In our case the patient aborted spontaneously; more often the foetus is unharmed and the pregnancy proceeds normally. Professor A. M. Claye, in a personal communication, has suggested that if a large dose of quinine did not produce abortion the foetus would escape serious harm. Nevertheless, it has seemed possible to us, in view of the wide range of sensitivity to this drug, that some unexplained examples of congenital blindness and/or deafness might be due to maternal ingestion of quinine for medicinal or abortifacient reasons.

Finally, it would appear desirable that quinine should be supplied to the public only on a doctor's prescription. Chemists with whom we have discussed this matter have assured us that quinine is rarely purchased nowadays, and only in small quantities, usually for the manufacture of home tonics and wines. Against this view is the fact that our own patient informed us that she had been advised to take quinine by a friend who had herself successfully aborted twice after taking ½ oz. (15.5 g.) of quinine on two separate occasions. Furthermore, a case of quinine poisoning was admitted under the care of one of us (L. G.) at the Royal Halifax Infirmary in December, 1952. This woman took an ounce (31 g.) of quinine sulphate by weight, having purchased it without difficulty at a multiple chemist's shop. She felt ill as soon as she had swallowed the powder, and vomited violently within the first five to ten minutes. She was seen within half an hour by her doctor, who rushed her into the Royal Halifax Infirmary, where the stomach was washed out. She never became completely blind, and her vision recovered fully within three weeks. Whilst writing this paper a further case of attempted abortion by quinine has come to our notice. This woman took an amount of quinine the "size of a sixpence" once weekly for the second two months of her pregnancy. She then gave it up and the foetus developed normally to term. It seems unlikely that our experience is unique. We have wondered whether this dangerous practice is not more common than is realized by the profession or by the pharmacist.

Summary

A case is recorded of complete blindness, of approximately forty hours' duration, due to the ingestion of quinine for abortifacient reasons. Drug therapy was ineffectual, but stellate ganglion block produced an immediate return of central vision and has probably favourably affected the degree of residual loss of peripheral vision. It is suggested that this treatment should be carried out immediately in all cases of retinal vascular spasm and especially in the treatment of thrombosis of the central retinal vein and embolism of the central retinal artery. The possible dangers to the foetus and the prevalence of the practice are discussed. It is recommended that restriction on the sale of quinine be imposed.

We wish to record our thanks to Mr. R. W. Hendry for his surgical assistance, to Mr. P. M. Wood for the ophthalmic assessments, and to Mr. Norman Emblin, who supervised the gynaecological aspects of the case.

REFERENCES

Braveman, B. L., *et al.* (1948). *Amer. J. Ophthal.*, **31**, 731.
Cotson, Tullos O. (1951). Ibid., **34**, 1289.
Duke-Elder, Sir W. S. (1940). *Textbook of Ophthalmology*, **3**, 3033.
King, E. F. (1934-5). *Proc. roy. Soc. Med.*, **28**, 354.
Leriche, R. (1952). *British Medical Journal*, **1**, 231.
Naffziger, H. C., and Adams, J. E. (1950). *Arch. Surg. (Chicago)*, **61**, 286.
Walsh, R. Crosbie (1954). *British Medical Journal*, **2**, 684.

RUPTURE OF UTERUS FOLLOWING ACCIDENTAL HAEMORRHAGE

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The incidence of rupture of the uterus is difficult to determine with any accuracy. It is particularly difficult to discover the incidence in Great Britain, as few large-scale reviews are reported, and the standard textbooks refer to series mainly from the United States of America. Brierton (1950) analysed eight large American series which reviewed 368 cases of uterine rupture occurring in 734,932 deliveries, an incidence of 1 in 1,997 cases. Watt (1950), from Canada, reported an incidence of 1 in 1,163 cases out of 17,455 deliveries. Simons (1950), from the Walton Hospital in Liverpool, recorded an incidence of 1 in 2,233 cases out of 33,492 deliveries, whilst the Rotunda Hospital (1952) figures were 1 in 1,333 deliveries. These figures seem to indicate that uterine rupture occurs once in every 1,500 to 2,000 deliveries, as is usually stated. All these figures are for hospital-managed cases. One wonders how truly representative these figures are, for as Titmus (1939) suggested, many cases of rupture are probably never diagnosed, being registered as deaths due to haemorrhage or shock.

Analysing 30 maternal deaths, Gordon and Rosenthal (1943) found at necropsy that 11 had a ruptured uterus, the diagnosis not having been made before death. Delfs and Eastman (1945) reviewed 17 cases of uterine rupture occurring in the absence of any uterine scar; in 23.6% the diagnosis was made post mortem. Sheehan (1948) reviewed 147 cases of obstetric shock: rupture of the uterus was found to be the cause in 20 cases.

The possibility of accidental haemorrhage causing rupture of the uterus is not considered by the majority of authors, although Powers and Gerard (1944) mention that in advanced pregnancy uterine rupture may be mistaken for premature separation of the placenta. Fraser (1954) describes two such cases in which a wrong diagnosis of concealed accidental haemorrhage was made, uterine rupture being discovered when a laparotomy was performed after the patients had failed to respond to conservative treatment. The presence of subperitoneal uterine haemorrhage following accidental haemorrhage has been noted many times. Uterine rupture may result when this process progresses a stage

further, especially in a uterus that has already been subjected to repeated caesarean sections.

A search through the index literature reveals only two cases of rupture of the uterus associated with accidental haemorrhage: Gibberd (1933) described a spontaneous complete rupture of the uterus occurring at the 28th week of a tenth pregnancy, the outcome being fatal. Gwillim (1933) described a similar case occurring at the 37th week of a second pregnancy; the patient survived. Gibberd was in no doubt that the sudden and increasing distension of the uterus was the cause of the rupture, although the multiparity of the patient and the thinness of the lower uterine segment must have been predisposing factors. No cause was found in the second case.

Case Report

A married woman aged 28 had previously had four lower-segment caesarean sections performed on account of diabetes mellitus. She was first found to have diabetes mellitus when she was 14 years old and had attended the hospital clinic for the past 11 years. The diabetic condition was well controlled on a 200-g. calorie diet and 20 units of soluble insulin morning and evening.

The first pregnancy was uneventful, lower segment caesarean section being performed at 36 weeks. The baby weighed 5 lb. 14 oz. (2.7 kg.) and died four hours after delivery, following a cyanotic attack. Post-mortem examination revealed atelectasis, but no foetal abnormalities.

Thirteen months later another caesarean section was performed at 36½ weeks. Some pre-eclampsia occurred in this pregnancy; the patient was in hospital for two weeks before delivery. The baby weighed 7 lb. 7 oz. (3.3 kg.) and caused no anxiety at any time.

The third caesarean section was performed 19 months later, at 36 weeks, following an uneventful pregnancy. The baby weighed 5 lb. 3 oz. (2.4 kg.) and died following a cyanotic attack 14 hours after delivery; no post-mortem examination was allowed.

The fourth caesarean section was performed at 36 weeks, the pregnancy having been complicated by a mild degree of pre-eclampsia. The presentation was a breech, and a type 1 placenta praevia was discovered at operation. The baby weighed 7 lb. (3.2 kg.) and at no time caused anxiety. After each operation the patient had a normal puerperium.

The present pregnancy had been uneventful except for a slight rise of blood pressure which had been noted at the clinic one week previously. By dates she was 34 weeks pregnant, there being no evidence of hydramnios.

The patient was admitted as an emergency, semi-comatose, shocked, and bleeding per vaginam. A history could not be obtained from her, but her husband gave a very full account of the happenings prior to admission. About 2 a.m. he awoke and noticed that his wife was sweating, and found that she was difficult to arouse. After taking a glucose drink she slept until 5 a.m., when again she was given a glucose drink as she was sweaty and drowsy. At 6 a.m. he gave her the usual dose of insulin. She did not have breakfast, but during the morning had two more glucose drinks. About midday he became more anxious because his wife was more drowsy. While dressing her he discovered that she was losing enough bright-red blood to produce a large stain in the bed. She did not complain of pain, but this was in all probability masked by the hypoglycaemic coma that was developing. Immediately after finding the bleeding the husband arranged for his wife to be admitted to hospital.

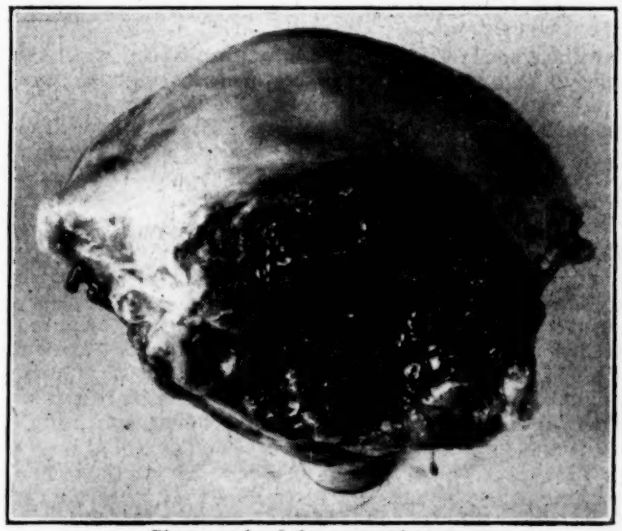
On admission to hospital on June 21, 1954, at 2.15 p.m., the patient was semi-comatose, extremely pale, and shocked: pulse rate 100, temperature 97° F. (36.1° C.), respirations 22, blood pressure 122/88. Abdominal palpation revealed a tense, woody-hard uterus, enlarged to the size of a 34-weeks pregnancy. The outline of the uterus was regular; no bulging or tenderness was discovered over the lower segment. The lie of the foetus was longitudinal; the presentation was not identified, nor was the foetal heart heard. Some bright-red blood was seen at the vulva. A diagnosis of hypoglycaemic coma and accidental haemorrhage was made. The blood sugar was 50 mg. per 100 ml., the haemoglobin was only 52%, and a catheter specimen of urine contained albumin.

While blood was being cross-matched a transfusion of "plasmosan" was started and 10 g. of glucose was given intravenously. Because at 4 p.m. the patient was becoming more restless she was given "omnopon," 1/3 gr. (22 mg.) intramuscularly, at the same time the blood transfusion was started. Two hours later she was much improved, her pulse was stronger and slower, and she had a drink containing 20 g. of glucose. The improvement continued until 9.30 p.m., when it was noted that her pulse rate was rising, and that she was becoming restless despite having had a further injection of omnopon, 1/3 gr. (22 mg.) intramuscularly. The slight bright-red blood loss was persisting, and the uterus was felt to be a little larger, softer, and much more tender, but still of regular outline, with no excess of tenderness over the lower segment. The blood pressure at this time was 140/100. It was thought that the uterus was becoming distended with blood from continued accidental haemorrhage.

By midnight the patient had become much more restless, and her pulse had risen to 120 beats a minute. Abdominal examination revealed a completely different picture. The uterus had previously been enlarged almost up to the xiphisternum, but now it was felt as a firm mass just below the umbilicus. The abdomen was seen to be distended, and everywhere was extremely tender. A pelvic examination revealed a slight blood loss; the cervix was closed. A diagnosis of rupture of the uterus was made, and the patient was prepared for immediate operation.

Caesarean Supravaginal Hysterectomy.—Under general anaesthesia the abdomen was opened, and immediately a large quantity of fresh blood was encountered. A complete rupture across the lower uterine segment at the site of the previous caesarean sections (see photograph) had allowed the foetus and placenta to escape into the peritoneal cavity. The foetus and placenta were removed from the right epigastric region together with a large blood clot and at least a pint (570 ml.) of fresh blood. Supravaginal hysterectomy was performed. At the end of the operation the patient's condition was satisfactory: blood pressure 122/88, pulse 120.

After an uninterrupted recovery she was discharged from hospital, on the 14th day. Subsequent examination of the uterus showed extensive infiltration of the uterine wall by a blood clot at the fundus in the region of the placental



Photograph of the ruptured uterus.

attachment. Blood extended through the uterine wall into the subsera, giving the typical appearance of a Couvelaire uterus. There was a complete rupture through the lower uterine segment at the site of the previous lower-segment caesarean section operations.

Discussion

Rupture of the uterus is a comparatively rare accident, and because of this it is often not considered as a diagnosis until the patient is moribund. Gordon and Rosenthal (1943) stressed that the failure to think of rupture of the uterus as a cause for cessation of contractions, absence of foetal heart sounds, shock during labour, or unaccountable shock after delivery may result in maternal death. Daniel and Inman (1951) advised exploration of the uterus in every case of persistent bleeding or shock following any major vaginal procedure, in order to eliminate a ruptured uterus. Watt (1950) emphasized that the diagnosis of complete rupture is usually made earlier than that of the incomplete variety. Incomplete rupture may present as a spreading haematoma, which may be unnoticed if it is posterior.

Cases of uterine rupture are divisible into three main categories, due to: (1) manipulative trauma, (2) rupture of a uterine or cervical scar, and (3) spontaneous rupture. In the first group inadequate antenatal care, misdiagnosis during labour, and, finally, unwise obstetrical manœuvres are largely responsible for the disasters. Cases of the second group mainly concern ruptured caesarean section scars, in particular those of classical and vertical lower-segment operations. A cervical tear in a previous labour may subsequently extend: Harris and Angawa (1951) report three fatalities due to high cervical tears. In the third group one finds that occasionally rupture occurs for no very good reason other than age, multiparity, and possibly dietetic deficiencies, as suggested by the experiments of Gillman *et al.* (1947), who noted that rats fed on certain deficient diets became more liable to rupture of the uterus.

Of recent years the vast improvements that have come about in the realms of anaesthesia, chemotherapy, and antibiotics have made caesarean section much safer. This has had the effect of increasing the number of caesarean operations performed, whilst at the same time tending to reduce the number of major obstetrical manœuvres undertaken. The effects of this swing away from heroic obstetrics in favour of caesarean section has shown itself to some degree when the causation of uterine rupture is considered. Improved obstetrical practice and fewer grand multiparae have reduced the number of uterine ruptures due to traumatic interference, but the increasing number of caesarean sections being performed does counterbalance this to some degree. The incidence of rupture of the scar following the classical operation is probably in the neighbourhood of 4%, as against 0.25% for the lower-segment operation (Wetterwald, 1926; Gellé, 1932).

Although the lower-segment operation is comparatively safe, in particular with reference to uterine rupture, there is a limit to the number of pregnancies that can be safely embarked upon in a uterus that contains an incision. The danger of the scar rupturing must increase with succeeding pregnancies, and more so in a uterus subjected to repeated sections.

Just how many pregnancies should be allowed is a very debatable point. Posner *et al.* (1951) state that tubal ligation is proposed to all their patients after two previous caesarean sections. Any statistics to illustrate the safety of pregnancy or the incidence of uterine rupture following caesarean section must obviously take this aspect into consideration. The incidence of hydramnios, pre-eclampsia, and foetal abnormalities in diabetic pregnancy is manifestly greater than in other pregnancies, and these complications can all be factors in the aetiology of uterine rupture.

These facts being evident, the wisdom of allowing a diabetic patient to have repeated pregnancies terminating in caesarean section must be doubted, as the risk of uterine rupture must be increased.

In the present case the fifth pregnancy was allowed to continue as the patient had only two living children from her four previous pregnancies, all the sections having been performed at the 36th week under ideal conditions and all the post-operative periods having been uneventful.

Reading through the literature one is impressed by the great variation in the way in which these cases present. Equally impressive is the manner in which some cases present with the minimum of symptoms and have been known to walk into hospital (Kerr and Moir, 1949). Walker (1950) described a case of lithopaedion formation following expulsion of the foetus into the peritoneal cavity after rupture of the uterus in labour.

After an accidental haemorrhage of even a small amount the general condition of the patient is usually poor. The case described presented just such a picture, complicated by hypoglycaemic coma. In hospital, with a blood transfusion and under sedation, the patient improved, and only some hours later, when her general condition was noticed to be deteriorating, was it discovered that the uterus had ruptured, there being no dramatic change in her condition.

Summary

A case of diabetic pregnancy complicated by accidental haemorrhage associated with spontaneous rupture of the uterus is described.

The difficulties of diagnosis are noted, with particular reference to that of distinguishing between accidental haemorrhage and uterine rupture.

Accidental haemorrhage is mentioned as being an aetiological factor in the causation of rupture of the uterus.

The diagnosis of shock following delivery is a dangerous one to make and should not be entertained without first exploring the lower uterine segment.

The correct diagnosis of uterine rupture will be made more often and more rapidly if the condition is kept in mind.

The danger of repeated caesarean section is discussed, with special reference to added complications of the diabetic pregnancy.

Early diagnosis, timely blood transfusion, prompt surgery, skilled anaesthesia, and the use of antibiotics should make the condition become less fatal than it is at the present time.

With the wider use of caesarean section, rupture of the uterus following internal version should become a great rarity.

The comparative rarity of grand multiparae, and the fewer classical caesarean sections that are performed, should reduce the incidence of uterine rupture.

I am indebted to Mr. J. H. Peel for permission to publish this case, and to Mr. W. Smith, of the photographic department of King's College Hospital, for the photograph.

REFERENCES

Brierton, J. F. (1950). *Amer. J. Obstet. Gynec.*, **59**, 113.
Daniel, W. W., and Inman, J. S., jun. (1951). *J. int. Coll. Surg.*, **16**, 706.
Delfs, E., and Eastman, N. J. (1945). *Canad. med. Ass. J.*, **52**, 376.
Fraser, D. (1954). *Proc. roy. Soc. Med.*, **47**, 119.
Gellé, P. (1932). *Bull. Soc. Obstét. Gynéc. Paris*, **21**, 62.
Gibberd, G. F. (1933). *Proc. roy. Soc. Med.*, **26**, 1159.
Gillman, J., Gilbert, C., and Gillman, T. (1947). *S. Afr. J. med. Sci.*, **12**, 153.
Gordon, C. A., and Rosenthal, A. H. (1943). *Surg. Gynec. Obstet.*, **77**, 26.
Gwillim, C. M. (1933). *Proc. roy. Soc. Med.*, **26**, 1160.
Harris, B. P., and Angawa, J. O. W. (1951). *J. Obstet. Gynaec. Brit. Emp.*, **58**, 1030.
Kerr, J. M. M., and Moir, J. C. (1949). *Operative Obstetrics*, 5th ed., p. 827. London.
Posner, L. B., Smith, D. F., and Trambert, H. L. (1951). *N.Y. St. J. Med.*, **51**, 641.
Powers, I. R., and Gerard, R. S. (1944). *J. Iowa St. med. Soc.*, **34**, 465.
Rotunda Hospital (1952). Clinical Reports. Dublin.
Sheehan, H. L. (1948). *Lancet*, **1**, 1.
Simons, P. (1950). *J. Obstet. Gynaec. Brit. Emp.*, **57**, 953.
Titmus, P. (1939). *Amer. J. Obstet. Gynec.*, **37**, 545.
Walker, A. H. C. (1950). *J. Obstet. Gynaec. Brit. Emp.*, **57**, 569.
Watt, G. L. (1950). *Amer. J. Obstet. Gynec.*, **59**, 490.
Wetterwald, M. (1926). *Zbl. Gynäk.*, **50**, 592.

FORCEPS DELIVERY UNDER LOCAL ANALGESIA

BY

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AND

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It has become increasingly evident in recent years that the use of general anaesthesia for forceps delivery is associated with a definite risk to the mother from aspiration of vomitus. Jeffcoate (1953) stated that the greatest danger of forceps delivery was anaesthesia and that this constituted the chief reason for advocating the use of local analgesia for all easy low-forceps deliveries. Parker (1954) reviewed the literature on maternal deaths from aspiration of vomitus, described five further cases, and showed that the risk of general anaesthesia, though small, was very definite. A plea was made for the wider use of local analgesia, "the safest of the common methods available." Other means of diminishing the maternal risk from this cause have been suggested by various authors. Among these are the stomach tube, spinal or caudal anaesthesia, chloroform, and the lateral position. All have disadvantages and dangers, and it seems to us that local analgesia is the safest of all.

In view of this we have used it for as many as possible of our forceps operations and have found it satisfactory not only for easy low-forceps deliveries but for a considerable number of more complicated cases.

The purpose of this paper is to describe a technique of injection and to assess the results of using it for forceps delivery.

Material and Selection of Cases

Out of a total of 105 consecutive forceps deliveries conducted personally by us, 65 (61.9%) were performed under local analgesia. The total is a combination of two smaller series drawn from two different hospitals. (1) East End Maternity Hospital, London : 33 cases (local analgesia 27, general anaesthesia 6). (All these cases were delivered by one of us.) (2) St. Mary's Hospitals, Manchester : 72 cases (local analgesia 38, general anaesthesia 34). It is proposed to assess the results of the 65 deliveries performed under local analgesia. The series included a large proportion of cases other than "low forceps" (Table I).

TABLE I.—*Distribution of* 105 *Cases*

Type	Local Analgesia	General Anaesthesia
Low	36	3
Mid	29	34
High	0	3
Total	65 (61·9%)	40 (38·1%)
Manual rotation:		
Occipito-posterior	4	11
Deep transverse arrest	2	13
Forceps rotation	2	4
Face to pubes	8	2

The outlook towards forceps delivery was conservative throughout. Thus forceps were never applied without strong indication and rarely before the cervix had been fully dilated for two hours. "Prophylactic" forceps delivery was never practised.

The selection of cases for local analgesia was made at the time when the need for intervention became apparent, and it involved general, abdominal, and vaginal examination. We were strongly biased in favour of local analgesia when there were features such as pulmonary or cardiac disease and in cases in which undue prolongation of labour had given rise to vomiting and ketosis. In these circumstances the risks of general anaesthesia were considered to be increased.

We avoided local analgesia when vaginal examination suggested that the rotation of the occiput or the actual extraction of the head was likely to be attended with considerable difficulty. Our one failure and the other unsatisfactory cases were all met with when the delivery proved to be difficult. We did not, however, hesitate to use the method simply because the head was above the ischial spine plane or because the position of the occiput was abnormal, and when the widest part of the head was past the ischial spines we used local analgesia almost invariably.

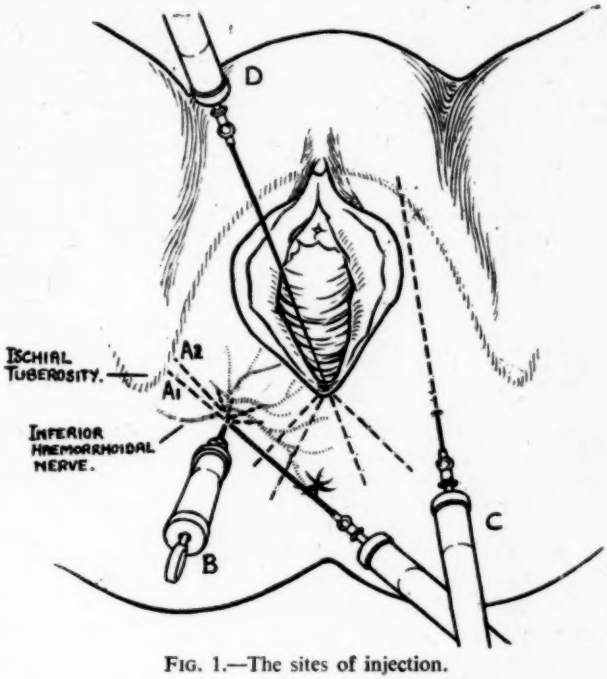

FIG. 1.—The sites of injection.

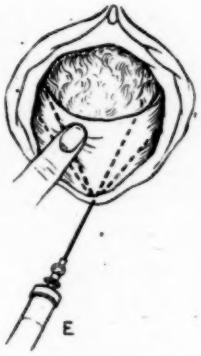

FIG. 2.—Labia separated to show the fanwise manner in which the mucosae of the posterior and lateral walls of the vagina are infiltrated.

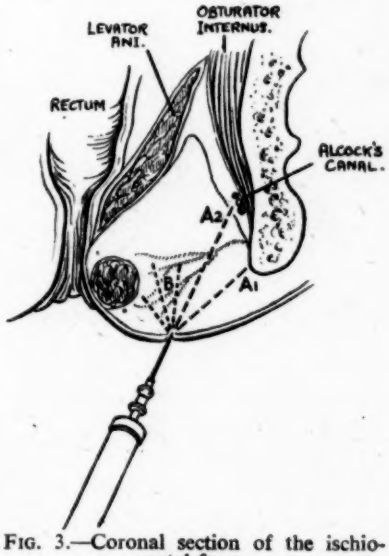

FIG. 3.—Coronal section of the ischio-rectal fossa.

Nervousness *per se* has not been a contraindication, and we have often been greatly surprised at the result of the method in highly excitable patients. Local analgesia is, however, impossible in the hysterical patient who will not lie still in spite of repeated reassurance.

Method

A technique was devised with the object of depositing the solution bilaterally in the following sites (see Figs. 1, 2, and 3) :

A. In the vicinity of the pudendal nerve as it traverses the pudendal (Alcock's) canal on the lateral wall of the ischio-rectal fossa. (The pudendal nerve has usually divided, before it reaches this level, into its two terminal branches—namely, the perineal nerve and the dorsal nerve of the clitoris. Both lie in Alcock's canal.)

B. Among the branches of the inferior haemorrhoidal nerve which pass medially across the ischio-rectal fossa to be distributed to the deep and subcutaneous portions of the external anal sphincter and to the skin between the anus and the ischial tuberosity. (The inferior haemorrhoidal nerve may have an independent origin from the sacral plexus or be a branch of the perineal or of the main trunk of the pudendal.)

C. Beneath the skin covering the lateral aspect of the labium majus as far anteriorly as the pubis, with the object of anaesthetizing the branches of the two superficial perineal nerves, the long perineal nerve of Soemmering, the ilio-inguinal nerve, and the genital branch of the genito-femoral nerve which supply the skin in this vicinity.

D. Beneath the skin of the perineum proper, including the line of the intended episiotomy.

E. Beneath the mucosa of the posterior and lateral walls of the vagina in its lower third.

The patient was first reassured. It is believed that this can make all the difference between success and failure. No mention was usually made of forceps, but the patient was told in general terms that it was proposed to inject some local analgesic, examine her, and if possible give her some assistance during her bearing-down efforts. In accordance with Smellie's (1751–2) teaching, the instruments were kept out of her sight. We used 80 ml. of 0.5% procaine (without adrenaline).

With the patient arranged in the lithotomy position and draped as for forceps delivery, a skin weal was raised on one side at a point midway between the anus and the ischial tuberosity. A 12-cm. lumbar-puncture needle on a 20-ml. syringe was pushed through the weal and directed antero-laterally so as to impinge on the bone at the mid-point of the medial surface of the ischial tuberosity, the latter being palpated through the skin with the left index finger (A1 in Figs. 1 and 3). The needle was then withdrawn slightly and directed towards a point 1 cm. medial and 3 cm. deep to the tuberosity (A2 in Figs. 1 and 3). Here the tip of the needle lay in Alcock's canal, and, after preliminary aspiration to ensure that a blood vessel had not been entered, 10 ml. of the solution was injected. The needle was then partly withdrawn and plunged at right angles to the skin, into the ischio-rectal fossa of the same side for a distance of 1½ to 2 in. (4–5 cm.), depending on the obesity of the patient. 10 ml. of the solution was then injected here (site B in Fig. 1), the needle being constantly moved about during the process. Without completely withdrawing the needle it was then redirected so as to lie beneath the skin covering the lateral aspect of the labium majus, its point reaching anteriorly almost as far as the symphysis pubis, and 10 ml. of the solution was injected, the needle being slowly withdrawn during the process (site C). The whole procedure was then repeated on the opposite side.

A further 10 ml. of solution was used to infiltrate the skin of the perineum proper, special attention being paid to the line of the intended episiotomy (site D). Finally 10 ml. was injected in a fanwise manner beneath the mucosa of the posterior and lateral walls of the lower third of the vagina, using the index finger of the left hand as a guide (site E in Fig. 2).

The time taken for the whole procedure was about five minutes. It can be seen that the method is essentially a combination of pudendal block and local infiltration analgesia. (A minor modification of the technique was used for some of the cases in that 0.5% lignocaine was used, and the pudendal nerve was blocked in the region of the ischial spine instead of in Alcock's canal.)

The patient was catheterized and the delivery proceeded with at once. All manipulations were performed very gently, more especially if rotation of the head was required. A right medio-lateral episiotomy was invariably performed, usually at an early stage. Traction on the forceps was exerted only during a labour pain, and the patient was encouraged to bear down at this time. (This is considered to be an important point. It is also of value at the time of crowning to tell the patient that the baby is being born, and that she will shortly hear it cry.)

Ergometrine, 0.5 mg., was given intravenously by an assistant as soon as the anterior shoulder of the foetus had been born. When the cord had been divided an immediate attempt was made to express the placenta. The episiotomy was repaired in the usual manner.

It is thought to be a mistake to give the patient any trichlorethylene or gas and air to breathe during the delivery, as this so dazes her that she may interpret non-painful stimuli as pain and become uncooperative.

Results

(1) *Maternal.—Mortality :* There was one maternal death (1.5%) in the series (Table II). This patient had severe mitral stenosis. She developed signs of rheumatic chorea and reactivation of rheumatic carditis shortly before delivery. She eventually died on the tenth day of the puerperium. *Post-partum haemorrhage :* Bleeding amounted to 20 oz. (570 ml.) or more in six cases (9.2%). *Manual removal of the placenta :* The placenta was retained on four occasions (6.2%) and required subsequent general anaesthesia for removal. *Episiotomy :* Healing of the perineum was unsatisfactory and required further treatment on three occasions (4.6%).

TABLE II.—*Mortality and Complications in the 65 Cases*

	No. of Cases	%
Maternal mortality	1	1·5
Corrected maternal mortality	0	0
Post-partum haemorrhage	6	9·2
Manual removal of placenta	4	6·2
Perineal complications	3	4·6
Foetal and neonatal mortality	2	3·1
Corrected foetal and neonatal mortality	0	0
Asphyxia neonatorum:		
Mild	10	15·4
Moderate	0	0
Severe	0	0

(2) *Foetal.—Mortality :* There were two stillbirths in the series (3.1%). In one case foetal death *in utero* had occurred two days before delivery because of post-maturity and pre-eclamptic toxaemia, and in the other case the foetus died 17 hours before delivery. The latter case was an emergency admission on account of prolonged labour, post-maturity, and intra-partum pyrexia. There were no neonatal deaths. *Asphyxia Neonatorum :* Mild asphyxia was noted on 10 occasions (15.4%). These babies responded within three minutes to simple treatment, and did not give rise to any anxiety.

(3) *Views of the Patients.*—The patients were questioned immediately after delivery or on the following day. Their reactions were classified as follows :

Satisfied	56 (86.1%)
Moderate discomfort but no pain	5 (7.7%)
Would have preferred general anaesthesia	4 (6.2%)

"Satisfied" was taken to mean that there had been no more discomfort than would have been expected during a normal delivery. None of these patients would have any fears about the prospect of a subsequent similar delivery. In many instances the patient was surprised to hear that she had had a forceps delivery. The nine less satisfactory cases were all encountered in those instances where more than an easy low-forceps delivery was performed.

(4) *Assessment of Operators' Reactions.*—The operator was entirely satisfied with the analgesia and relaxation in 53 of the cases (81.5%). In only one case (1.5%) was the procedure a complete failure and resort made to general anaesthesia. In the remaining 11 cases (17%) the only objection was lack of co-operation in patients, most of whom ultimately denied undue discomfort.

Discussion and Conclusions

There was one maternal death in the series. This was, however, unavoidable and in no way due to the analgesic. The risk of maternal death as a direct result of general anaesthesia is, on the other hand, sufficiently well known to need no substantiation, and it is probable that this risk is higher where skilled anaesthetists are not available. The incidence of post-partum haemorrhage and of manual removal of the placenta was lower than might have been expected in a comparable series under general anaesthesia. The latter has a well-known adverse effect on uterine contraction and retraction. The incidence of perineal complications was low, and this has done much to allay our fears that local injections around the lower birth canal might increase the sepsis rate and interfere with sound healing.

There were no foetal or neonatal deaths attributable to the delivery, and in no case was any anxiety experienced on account of asphyxia neonatorum. General anaesthesia is a potent cause of the latter, and we have been greatly impressed by the immediate breathing and crying of infants delivered under local analgesia. The incidence of mild asphyxia was somewhat higher than we had expected. This may be a result of the high proportion of unbooked cases admitted because of prolonged labour (7 cases, 10.8%).

It is suggested that local analgesia, used in the manner described, can obviate the risks of general anaesthesia without introducing any new hazards. It is probable that general anaesthesia is still used for the majority of low-forceps deliveries performed in this country, and it seems to us that a much wider use of the local analgesic method is justifiable. Our own experience further suggests that the scope of the method is not limited to low-forceps operations. Thus, while 92.3% of our low-forceps deliveries were performed under local analgesia, 46% of our mid-forceps deliveries were likewise conducted; and of all our cases requiring rotation of the occiput, 22.2% were delivered under local analgesia.

The patient was satisfied in 86.1% of cases, the operator in less (81.5%), and this is as it should be. It should, however, be noted that if the method is limited to low-forceps deliveries the success rate is almost 100%.

The technique should have a valuable place in domiciliary practice. It is not difficult to learn (demonstration is not essential), and it is possible to conduct the delivery single-handed and in a leisurely manner. The term "failed forceps" would lose its serious import, and the fierce determination to deliver that can at times assail the most level-headed obstetrician would be largely forestalled. One of the advantages of the method is that it makes gentleness of manipulation mandatory.

We are aware that the use of local analgesia would present certain difficulties in domiciliary practice. It would be necessary to maintain a supply of reasonably fresh analgesic solution, and a sterile syringe and needles would have to be kept in a special box.

We believe that these difficulties could be overcome and that the disadvantages they represent are far outweighed by the many advantages of the method. Although we prefer the lithotomy position where this is possible, we have used the method for forceps deliveries in the left lateral position and found it to be entirely practicable and satisfactory. All our cases were given ergometrine intravenously, but we do not believe that this is essential.

It is generally agreed that, except where transfer of the patient to hospital is contraindicated, nothing more extensive than a low-forceps delivery should be contemplated in the patient's home; and local analgesia should therefore be almost universally applicable in these circumstances.

Summary

The need for safer anaesthesia for forceps delivery is recognized.

A method of injection is described.

The results of 65 forceps deliveries under local analgesia are discussed.

A wider application of the method is recommended, especially in domiciliary practice.

We are grateful to the following consultants, under whose care the cases were admitted, for their permission to publish our results: Dr. K. V. Bailey, Mr. D. G. Wilson Clyne, Dr. E. A. Gerrard, Dr. J. W. A. Hunter, Professor W. I. C. Morris, Dr. R. Newton, Mr. B. G. Spiers, and Dr. A. H. C. Walker. We wish to thank Professor Morris for his criticism and advice. We are indebted to Miss D. Davison for the drawings.

REFERENCES

Jeffcoate, T. N. A. (1953). *British Medical Journal*, **2**, 951.
Parker, R. B. (1954). Ibid., **2**, 65.
Smellie, W. (1751-2). *Treatise on the Theory and Practice of Midwifery*, vol. 1. London.

ACUTE LEUKAEMIA IN PREGNANCY

REPORT OF A CASE

BY

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Forkner (1938), reviewing the literature, was able to find reports of 53 cases of all types, in 5 of which the diagnosis was doubtful. Grier and Richter (1939) collected 75, while Moloney *et al.* (1943), presenting one of chronic myeloid type, increased the total to 79. Adding another five to this number, Almklov and Hatoff (1946) reported the tenth published instance of acute lymphatic leukaemia in pregnancy. Erf (1947) published a summary of 100 cases of leukaemia in pregnancy, including two of chronic myeloid leukaemia which he personally observed. His figures for the different forms of leukaemia were: acute myeloid, 24; chronic myeloid, 63; acute lymphatic, 10; chronic lymphatic, 3.

Since 1947 the occurrence of leukaemia in pregnancy has been reported a further 17 times. On three occasions (Williams, 1948) the disease was of the acute type, one being acute lymphatic leukaemia; and Shub *et al.* (1953) described a case of chronic myeloid leukaemia which became acute during pregnancy. Allan (1954) reported four new cases of chronic myeloid leukaemia. Thus there has been reference in the literature to 38 instances of acute leukaemia in pregnancy, and 11 of these were of the acute lymphatic variety.

Case Report

The patient, aged 41, was admitted to the antenatal ward in July, 1954, because of increasing pallor, general fatigue, and swelling of the ankles. She was in the thirty-fifth week of pregnancy. The children of three previous normal pregnancies were alive and well. She had a miscarriage in 1940 at four months, preceded by appendicitis, complicated by peritonitis. Her health had been good until the fifth month of the present pregnancy.

Examination revealed a pale woman with a few purpuric spots on the right leg, both legs being oedematous. Her gums and throat were healthy, the liver and spleen could not be palpated, but there were a few palpable cervical and axillary glands and the sternum was acutely tender to pressure. The blood pressure was normal, the urine clear, and she was apyrexial. Haematological investigation on August 19 revealed: haemoglobin, 10.8 g.%; P.C.V., 28%; M.C.H.C., 26%; leucocytes, 68,400 per c.mm.; platelets, 160,000 per c.mm. Examination of a stained blood film showed notably a large number of blast cells. The red cells appeared normal. The differential leucocyte count showed: blast cells, 68%; large lymphocytes, 16%; small lymphocytes, 9%; neutrophil polymorphs, 6%; neutrophil myelocytes, 1%. The sternal marrow smear showed extreme cellularity, and consisted almost entirely of blast cells. A few normoblasts and an occasional megakaryocyte were seen. On the basis of the above findings a diagnosis of acute (lymphoblastic) leukaemia was made.

The patient was delivered of a live, healthy male child on August 27 by elective lower segment caesarean section. Unfortunately the placenta was not retained for microscopical examination, but macroscopically it showed no abnormality. The operation was not attended by excessive bleeding, although the surface of the uterus was noted to bruise readily. Post-partum progress was uneventful apart from persistent pyrexia and increase in the degree of anaemia. Complete examination of the infant's cord and venous blood revealed no abnormal features.

Five days after delivery the patient was transferred to a medical ward. Her main complaints were lack of appetite and burning retrosternal discomfort on swallowing. The spleen was now palpable one fingerbreadth below the left costal margin. Ophthalmoscopy revealed no abnormality. The haemoglobin was 6.5 g.%, the platelet count had fallen to 90,000 per c.mm., and the clotting and bleeding times were normal.

On September 10 treatment with oral cortisone acetate in dosage of 25 mg. four times daily was begun, without producing any improvement in her haematological state. The patient left hospital at her own request on September 18, treatment having been discontinued.

On September 23 she was readmitted to the gynaecological department because the abdominal wound had broken down. Treatment with 6-mercaptopurine was followed by a haematological remission on two occasions, and she left hospital on December 3 with the abdominal wound well healed. Unfortunately, permission for further marrow examination was not obtained, but examination of the peripheral blood showed a significant change. On December 1 the leucocyte count was 3,000 per c.mm., and only 1% blast cells were seen in the stained blood film.

Discussion

Four aspects of the problem of acute leukaemia in pregnancy may be considered.

1. *Effect of Pregnancy on the Leukaemic Process.*—From reference to the literature it is clear that there is no evidence that pregnancy has either a favourable or an unfavourable influence on acute leukaemia. Erf (1947) noted that of 34 cases of acute leukaemia those who survived delivery did not live longer than three months, while out of 66 cases of chronic leukaemia 43 patients survived pregnancy by more than one year, and several had more than one pregnancy. The survival times do not differ from those in non-pregnant leukaemic patients. Shub *et al.* (1953) suggest that pregnancy may transform chronic leukaemia into the acute form, but the history and clinical state of the present case indicate that the disease was acute from the onset.

2. *Effect of Leukaemia on Pregnancy.*—The most common result of leukaemia in pregnancy is premature labour. Almklov and Hatoff (1946) concluded that the association of pregnancy and acute leukaemia resulted in a high foetal mortality, less than 50% of infants being successfully delivered. It is more likely that acute leukaemia will develop during pregnancy than that a patient suffering from acute leukaemia will become pregnant. If the disease begins early in pregnancy the chances of a live child are extremely remote, unless the mother has a remission, either spontaneous or induced. When it occurs late in pregnancy, as in the present instance, the production of a live child is more probable.

3. *Effect of Leukaemia on the Child.*—In no case of leukaemia in pregnancy has there ever been reported transmission of the disease to the child. While there have been at least 21 published cases of congenital leukaemia (Wintrobe, 1951), in no instance was the mother affected, and leukaemic cells were demonstrated only on the foetal side of the placental barrier. No foetal abnormalities have ever been directly related to leukaemia in the mother.

4. *Management of the Patient.*—Acute leukaemia is a fatal disease with a rapid course, and treatment is normally a matter of academic and research interest. Where pregnancy coexists, however, there is the problem of producing a live child, and treatment of the patient will require special consideration. The folic-acid antagonists induce remission, mainly in children, and this is probably true also of 6-mercaptopurine (Burchenal *et al.*, 1953). Improvement has sometimes been produced in adults with the latter drug (Hall *et al.*, 1953), and in the early months of pregnancy it would seem reasonable to use these drugs in the hope that a remission may be induced long enough to allow pregnancy to run a normal course. It should be remembered, however, that the effect of the antimetabolites on developing foetal tissues is unknown, and for this reason, in the late stages of pregnancy where the course of the illness is not a fulminating one, it is probably justifiable to withhold therapy of a specific nature and to rely on supportive measures such as blood transfusion and antibiotics, as was done in this patient.

Where thrombocytopenia is present with its attendant risk of haemorrhage, platelet transfusion or that of polycythaemic blood may be a valuable measure.

The management of labour constitutes another problem. Haemorrhage may be a hazard, and its treatment has been referred to. In general, the mother should be delivered, where possible, by the normal route. In the present case caesarean section was performed only when surgical induction had failed. The failure of the abdominal wound to heal may be attributed either to the leukaemic process or to the use of cortisone.

Summary

The twelfth reported case of acute lymphatic leukaemia in pregnancy is described, a live healthy child being delivered by caesarean section. Some of the problems of management are discussed.

I wish to thank Dr. J. L. Markson for his encouragement and advice, and Dr. J. B. Rennie and Dr. D. McK. Hart, under whose care this patient was treated, for permission to publish.

REFERENCES

Allan, J. (1954). *British Medical Journal*, **2**, 1080.
Almklov, J. R., and Hatoff, A. (1946). *Amer. J. Dis. Child.*, **72**, 202.
Burchenal, J. H., Murphy, M. L., Ellison, R. R., Sykes, M. P., Karnofsky, D. A., Leone, L. A., Tan, T. C., Craver, L. F., Dargeon, H. W., and Rhoads, C. P. (1953). *Blood*, **8**, 965.
Erf, L. A. (1947). *Amer. J. clin. Path.*, **17**, 268.
Forkner, C. E. (1938). *Leukaemia and Allied Disorders* (Bibliography). Macmillan Co., New York.
Grier, R. M., and Richter, H. A. (1939). *Amer. J. Obstet. Gynec.*, **37**, 412.
Hall, B. E., Richards, M. D., Willett, F. M., Feichtmeier, T. V., and Aggeler, P. M. (1953). *Stanford med. Bull.*, **11**, 237.
Moloney, W. C., Heffernan, R. J., and Kasdon, S. C. (1943). *J. Amer. med. Ass.*, **122**, 1170.
Shub, H., Black, M. M., and Spear, F. D. (1953). *Blood*, **8**, 375.
Williams, J. A. (1948). *Amer. J. Obstet. Gynec.*, **55**, 967.
Wintrobe, M. M. (1951). *Clinical Haematology*, 3rd ed., p. 857. Kimpton, London.

CONTROLLED HYPOTENSION WITH ARFONAD IN PAEDIATRIC SURGERY

BY

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Since the methonium compounds were first used to lower the blood pressure during surgery (Organe, 1950; Davison, 1950; Enderby, 1950; Shackleton, 1951) a fairly extensive literature has accumulated on controlled hypotension. The effects of other ganglion-blocking agents have been reported, the last being pentolinium tartrate (Enderby, 1954). The short-acting agent "arfonad" was first reported in American literature by Nicholson *et al.* (1953) and Sadove *et al.* (1953), and in this country by Magill *et al.* (1953), Anderson and McKissock (1953), Scurr and Wyman (1954), and Kilduff (1954). In some of these papers the mode of action of arfonad and its advantages over other ganglion-blocking drugs are described, and are therefore not repeated.

In previous literature it has been shown that, weight for weight, children are more tolerant of the depressant and the relaxant drugs used by anaesthetists than are adults (Anderson, 1951). The purpose of this paper is to show that children are also tolerant of the drugs used to produce hypotension, and that the technique of controlled hypotension can be used in the surgery of children with no greater danger than in adults.

Reports on the use of the hypotensive drugs have so far been concerned mainly with adults. Of the 250 cases reported by Scurr and Wyman, only two were under 10 years of age. Kilduff includes three children under 10 in his series of 10 cases. These authors stressed the resistance shown by young adults to the ganglion-blocking agents. This paper stresses the resistance shown by children. Although the present series is small (44 children in 18 months), it is thought that it provides enough information for certain conclusions to be reached. The reason why there are not more cases is the obvious one: there are not many occasions when both the surgeon and the anaesthetist are confident that the hazards of using the hypotensive technique are more than outweighed by the surgical risk without it. But in neurosurgery and in certain cases requiring careful plastic reconstruction the use of controlled hypotension has proved invaluable. Of the 44 children 29 were under 7 years old (Table I).

TABLE I.—*Analysis of 44 Cases*

Age in Years	Type of Surgery		
	Neurosurgery	Genito-urinary	General
5/12		1	
8/12		1	
11/12		1	
1	2	3	
2	3	1	
3	4	1	
4			1
5	2	1	2
6	4		2
7	3		
8	2	1	
9	1		
10	2		
11	2	1	1
12	1	1	
	26	12	6

Technique

I believe that arfonad delivered by drip transfusion is the method of choice for inducing hypotension in children, because of the great flexibility of control so obtained. That arfonad needs to be administered by drip transfusion seldom proves to be a disadvantage in practice, for paediatric surgery which demands controlled hypotension also requires, as a rule, a cut-down drip transfusion for replacing blood loss. The methonium compounds were used before supplies of arfonad were made available for trial, but the results were not satisfactory. The child, like the young adult, proved very resistant to these drugs, with the result that when hypotension was produced it lasted for so short a time that repeat doses were often needed. These repeat doses produced tachyphylaxis, so that procainamide was added in an attempt to keep the blood pressure down to the required level.

The first important observation to be made was any change in the systolic blood-pressure reading after the table had been tilted. This was often a useful guide to the patient's reaction to arfonad. The drip was run slowly at first, for it was found easier to control the blood pressure if this was allowed to fall gradually from the beginning.

Strength of Solution

So variable is individual reaction to these drugs that it has proved difficult to find the most suitable strength of solution. That used for adults is usually 0.1% (1 mg. per ml.). The tendency early in this series was to use too weak a solution. This carried the risk of overloading the child with fluid in order to keep the pressure down to the required level. For example, Case 14 (a child of 6) required a drip rate of 160 in order to keep the pressure between 60 and 70 mm. Hg systolic (Table II). The strength of the solution was then doubled to 0.2% (2 mg. per ml.), when this blood-pressure level could be maintained at a drip rate of between 8 and 16 drops a minute. Case 12 (also a child aged 6) required a triple-strength solution 0.3% (3 mg. per ml.) to keep the systolic blood pressure between 60 and 70 mm. Hg with a drip rate varying between 14 and 20 drops a minute.

The present practice is to use the 0.1% solution of arfonad for infants and children up to 5 years old. A double-

TABLE II

Case No.	Age in Years	Operation	Operating Time (Minutes)	Total Arfonad Used (mg.)	Strength of Solution (mg./ml.)	Drip Rate (Drops/min.)
1	5/12	For ectopic bladder	90	10	1·0	8–16
2	8/12	,, ,,	110	80	0·5	12–58
3	11/12	Cystectomy	130	45	1·0	5–10
4	1	For ectopic bladder	100	55	0·5	20–30
5	2	Craniotomy	50	190	1·0	53 (average)
6	2	,,	60	50	0·5	28 ,,
7	2	For ectopic bladder	120	270	2·0	12–48
8	3	,, ,,	45	5	0·5	10
9	3	Craniotomy	50	90	1·0	40
10	3	,,	90	25	1·0	8–32
11	5	,,	75	50	1·0	3–40
12	6	Recto-sigmoidectomy	120	222	3·0	14–20
13	6	Craniotomy	90	14	1·0	16–48
14	6	,,	130	280	1·0 2·0	30–140 8–16
15	6	,,	75	140	1·0	10–80
16	7	,,	100	25	1·0	16–20
17	7	,,	40	21	2·0	8
18	7	,,	70	220	2·0	24–44
19	8	,,	35	120	1·0	30–50
20	9	,,	60	500	2·0	70 (average)
21	11	,,	210	250	1·0	10
22	11	Plastic to genitalia	60	250	1·0 2·0	40–60 12–48
23	11	Craniotomy	50	90	1·0	20–40
24	12	Plastic to urethra	150	250	1·0	28 (average)
25	12	Craniotomy	120	160	1·0	6–60

Full data were recorded in only 25 out of the 44 cases.

strength solution, 0.2%, is given to children of 6 years and upwards. The strength of the solution is increased still further if hypotension can be maintained only with an excessive drip rate.

Results

Satisfactory hypotension was produced together with improved operating conditions in every case.

Five of the first 20 cases received procainamide because a suitably low blood pressure could be maintained only with an excessive drip rate. Since the use of stronger solutions of arfonad (in 24 cases) procainamide has not been given.

There was no operative death in the series. One child, aged 4 (who had thyroidectomy for thyrotoxicosis), died within 24 hours of operation from acute heart failure, having been extremely well post-operatively, and talking to a nurse a few minutes before her death. One of the infants caused temporary alarm during the operation when the pulse became imperceptible owing to the drip being accidentally accelerated.

Blood loss was replaced whenever considered necessary (three cases).

In only two cases was a vasopressor drug used; this was given to raise the blood pressure quickly to identify and control bleeding-points before closing the dura mater. In all the other cases the blood pressure returned to near normal levels within a few minutes of stopping the arfonad and levelling the table.

Summary

A series of 44 children is presented in which surgery was performed under controlled hypotension induced by arfonad. An analysis of these cases is shown in tables.

It is concluded that controlled hypotension can be used in paediatric surgery, when indicated, with no greater danger than in adult surgery.

The tolerance of the child raises certain problems in technique of administration, which are described.

The value of the flexibility of action of arfonad when given by drip transfusion is emphasized.

My thanks are due to Mr. Wylie McKissock, Mr. D. Innes Williams, and Mr. George MacNab for permission to record the cases on which this report is based, and to Roche Products Limited, who kindly supplied the arfonad.

REFERENCES

Anderson, S. M. (1951). *Lancet*, **2**, 965.
—— and McKissock, W. (1953). Ibid., **2**, 754.
Davison, M. H. A. (1950). Ibid., **1**, 252.
Enderby, G. E. H. (1950). Ibid., **1**, 1145.
—— (1954). Ibid., **2**, 1097.
Kilduff, C. J. (1954). Ibid., **1**, 337.
Magill, I. W., Scurr, C. F., and Wyman, J. B. (1953). Ibid., **1**, 219.
Nicholson, M. J., Sarnoff, S. J., and Crehan, J. P. (1953). *Anesthesiology*, **14**, 215.
Organe, G. (1950). *Proc. roy. Soc. Med.*, **43**, 181.
Sadove, M. S., Wyant, G. M., and Gleave, G. (1953). *Anaesthesia*, **8**, 175.
Scurr, C. F., and Wyman, J. B. (1954). *Lancet*, **1**, 338.
Shackleton, R. P. W. (1951). *British Medical Journal*, **1**, 1054.

It was a hundred years ago that JOHN SNOW, well known as an anaesthetist, asserted that a cholera epidemic raging in London would cease if the handle of a pump in Broad Street (now Broadwick Street), Soho, were removed. He was gathering evidence that cholera is a water-borne disease, and found that all the infected persons in this epidemic had drawn water from the Broad Street pump. The epidemic, which had caused 500 deaths in 10 days, stopped immediately the pump was put out of action. Hard by where the pump once stood is now a public house, and, in response to a request that this landmark in epidemiology should be commemorated, the owners, Messrs. Watney, Combe, Reid and Co., agreed to change its name from the "Newcastle On Tyne" to the "John Snow." The occasion was celebrated on July 5 when Professor BRADFORD HILL, F.R.S., before a gathering of epidemiologists, recalled these events and unveiled the new inn sign depicting John Snow. Some mementoes of Snow are now on permanent view at the premises.

THE POTENTIATION OF BARBITURATE ANAESTHESIA BY DINITRO-*O*-CRESOL

BY

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Our attention was recently drawn to the findings of Bain (1952) and Brody and Bain (1954) that a wide range of barbiturate drugs exhibit *in vitro* dissociating effects on oxidative and phosphorylating processes in liver and brain mitochondria, qualitatively similar to, although quantitatively less than, those produced by dinitrophenol (D.N.P.). Bain also stated in a footnote that barbiturate anaesthesia in rats and mice was potentiated by dinitrophenol, while Brody and Bain showed that the effects of thiobarbiturates on mitochondrial preparations more closely resembled those of D.N.P. than did those of oxygen barbiturates.

The widely used agricultural herbicides dinitro-*ortho*-cresol (D.N.C.) and dinitro-*sec*-butylphenol (D.N.B.P., "dinoseb") have a mode of toxic action almost indistinguishable from that of D.N.P., and are sufficiently hazardous in agricultural usage to present a distinct possibility of occupational poisoning. Sedation by oral or parenteral barbiturates has hitherto been advised to allay any dangerous restlessness or excitement which may occur in such cases (Bidstrup and Payne, 1951; B.M.A., 1951; Martindale, 1952; Edson, 1955). There also exists the possibility that a case of mild or even severe D.N.C. intoxication may require the induction of surgical anaesthesia for some essential operative procedure, such as the treatment of physical injuries. A series of experiments has therefore been carried out to compare the responses of normal and D.N.C.-poisoned animals to the narcotic effects of six representative barbiturates.

Materials and Methods

The animals used were adult male and female albino rats of Glaxo-Wistar strain, acclimatized to our laboratory conditions (67–76° F. (19.5–24.5° C.) during the experimental period) and maintained on M.R.C. Diet No. 41. D.N.C. was administered intraperitoneally as a 1% solution of the sodium salt, the dose mainly used (17–20 mg./kg.) being that known from previous work to cause moderate to severe D.N.C. poisoning with an expected 20–30% mortality, under our experimental conditions. (In order to maintain a direct check on this point, a "D.N.C. control group" was included in all but one of the trials. The mortality in these 48 animals was 29%.)

The oxygen barbiturates investigated were pentobarbitone ("nembutal," intraperitoneally), hexobarbitone ("cyclonal," intravenously), amylobarbitone ("amytal," i.v.), and phenobarbitone ("gardenal," i.v.), the thiobarbiturates being thiopentone ("pentothal," i.v.), and thialbarbitone ("kemithal," i.v.). All were administered as freshly prepared solutions of the sodium salts, injections being carried out by one person, with due care to avoid any marked variation in the speed of injection into individual animals and in the experimental groups.

Preliminary trials with each barbiturate indicated the dosage likely to cause a degree of narcosis with a readily recognizable onset and duration. A state of deep flaccid "surgical" anaesthesia was sought in most trials, since

restoration of muscular tone and slight stirring movements on disturbances were then "end-points" comparatively easily recognized. With intraperitoneal pentobarbitone and with amylobarbitone, less deep degrees of narcosis were employed. Observations on onset, depth, and duration of narcosis were made by one observer. In general, the individual response among the controls for each barbiturate was so uniform that it was considered justifiable to use group mean times of onset and duration of narcosis in the comparisons.

Each barbiturate was investigated by comparing the effects of a "high" barbiturate dose in normal control animals and in animals suffering from moderate to severe D.N.C.-intoxication. The use of comparatively high dosages both of D.N.C. and of barbiturate was intended to simulate the use of the latter to induce surgical anaesthesia or to combat marked excitement in a case of D.N.C.-poisoning.

Further tests were then carried out on small groups of animals to determine if a reduced dose of intravenous thiopentone was significantly potentiated by a high dose of D.N.C., or if an anaesthetic dose of thiopentone was potentiated by an almost asymptomatic dose of D.N.C.

The experimental programme obviously did not cover the many possible variants of drug dosage and combination, and was carried out on only one species. Nevertheless the nature of the results obtained appears to justify early publication.

Results and Discussion

The accompanying Table gives details of the actual dosages of D.N.C. and barbiturate employed, group numbers and mortalities, approximate times of onset and duration of narcosis, and a summary of the conclusions drawn from each experiment.

The series showed clearly that, with the exception of hexobarbitone, the narcotic effect of the barbiturates tested was markedly potentiated by the presence of severe D.N.C. intoxication. Deeply anaesthetizing but normally non-fatal doses of both thiopentone and thialbarbitone were lethal in D.N.C.-poisoned rats. Most such animals developed deep cyanosis within seconds of thiobarbiturate injection, dying immediately or within a few minutes after respiratory and then cardiac arrest. Of the four oxygen barbiturates examined pentobarbitone, amylobarbitone, and phenobarbitone were all potentiated by D.N.C.-poisoning, as judged by the greater rapidity of onset, depth, and duration of their narcotic effects. Potentiation was not demonstrated with hexobarbitone under similar conditions. This observation may be explained by the finding of Brody and Bain that hexobarbitone ("evipan") caused appreciably less *in vitro* dissociative effect upon mitochondrial oxidative-phosphorylating processes than the other twelve barbiturates investigated by them.

The results obtained also suggested that barbiturate potentiation is only likely to occur with D.N.C. dosages high

Effects of Barbiturate Drugs in Normal and in D.N.C.-treated Rats

Compound (as Na Salt) and Route	Dose (mg./kg.)	No. in Group	% Mortality (7 Days)	Narcosis Produced*			Survival Times	Potentiation of Barbiturate Effects	Remarks
				Depth	Onset (min.)	Duration (min.)			
Phenobarbitone i.p.	20	12	0	Moderate	5–15	60–90	—		
D.N.C. i.p.	20	16	25	—	—	—	1–3 hrs.		
Phenobarbitone i.p. concurrently with D.N.C. i.p.	20 / 20	16	37	Deep	2–3	120–180	1–12 „	+	
Hexobarbitone i.v.	40	16	0	Deep	Immediate	20–30	—		No apparent influence of D.N.C. on barbiturate anaesthesia
D.N.C. i.p.	20	12	33	—	—	—	1–3 hrs.		
Hexobarbitone i.v. 5–15 min. after D.N.C. i.p.	40 / 20	12	42	Deep	Immediate	20–30	1–2 „	–	
Amylobarbitone i.v.	60	8	37	Deep	3–5	180	1–2 hrs.		Dosage of both amylobarbitone and D.N.C. too high. Barbiturate after D.N.C. produced immediate cyanosis and prompt death in 4/7 animals. Survivors not cyanosed
D.N.C. i.p.	20	4	100	—	—	—	½–2 „		
Amylobarbitone i.v. 5–15 min. after D.N.C. i.p.	60 / 20	7	57	Deep	½–1	180–300	1–20 min.	+	
Amylobarbitone i.v.	40	4	0	Moderate to mild	10 (2)	25 (2)	—		No cyanosis produced at these reduced dosages
D.N.C. i.p.	17	4	0	—	—	—	—		
Amylobarbitone i.v. 5–15 min. after D.N.C. i.p.	40 / 17	4	0	Deep	2–14	60–90	—	+	
Phenobarbitone i.v.	100	8	0	Deep	20	120	—		
Phenobarbitone i.v. 5–15 min. after D.N.C. i.p.	100 / 20	8	12	„	10	240–360	20 min.	+	
Thialbarbitone i.v.	80	6	0	Deep	Immediate	20–35	—		Immediate cyanosis and rapid death after barbiturate in D.N.C.-treated group. No cyanosis after thialbarbitone alone
D.N.C. i.p.	20	4	25	—	—	—	—		
Thialbarbitone i.v. 5–15 min. after D.N.C. i.p.	80 / 20	4	100	Deep	Immediate	Fatal	< 1 min.	++	
Thialbarbitone i.v.	40	7	0	Moderate	Immediate	3–5	—		No cyanosis produced at this reduced thialbarbitone dosage
Thialbarbitone i.v. 5–15 min. after D.N.C. i.p.	40 / 20	4	25	Deep	„	10–23	1 hr.	++	
Thiopentone i.v.	10	8	0	Mild	Immediate	3–5	—		Immediate cyanosis and rapid death in 7/8 animals after barbiturate in D.N.C.-treated group. No cyanosis in survivor
	30	8	0	Deep	„	34	—		
D.N.C. i.p.	20	8	12	—	—	—	1½ hrs.		
	10	4	0	—	—	—	—		
Thiopentone i.v. 5–10 min. after D.N.C. i.p.	30 / 20	8	88	Deep	Immediate	90 (1 survivor)	1–20 min.	++	
Thiopentone i.v. 5–10 min. after D.N.C. i.p.	30 / 10	4	0	Deep	Immediate	25	—	–	Duration of narcosis similar to that in thiopentone control group at 30 mg./kg.
Thiopentone i.v. 5–10 min. after D.N.C. i.p.	10 / 20	4	0	Mild to moderate	Immediate	10	—	+	

*Deep: Flaccid anaesthesia. Moderate: Inert, but muscle tone still present. Mild: Weakness, ataxia.

enough to cause characteristic signs of poisoning and profound disturbances of cellular oxidation-phosphorylation processes. Low D.N.C. dosage did not appear to potentiate high thiopentone dosage, whereas high D.N.C. dosage did appear to potentiate even quite low thiopentone dosage. The distribution of characteristic deaths due to D.N.C. was fairly equal in the D.N.C.–barbiturate and D.N.C. control groups, the implication being that, although high D.N.C. dosage potentiated the effects of all but one of the barbiturates tested, the barbiturates did not under these conditions potentiate or mitigate the toxicity of D.N.C.

We have been unable to find any instances in the published literature of severe D.N.C.-poisoning in humans being treated by sedation by barbiturate drugs, although in their report on a case of severe but non-fatal D.N.C.-intoxication Pollard and Filbee (1951) refer to sedation as part of the treatment adopted. During the past three years no cases of fatal or serious D.N.C.-poisoning have occurred in this country, so perhaps the therapeutic problem of D.N.C.–barbiturate synergism has not yet occurred in practice. It is worth noting, however, that D.N.P. itself still has some industrial use in the chemical and explosives industries, and that Brody and Bain also found that chlortetracycline ("aureomycin"), thyroxine, and methadone have considerable dissociating properties *in vitro*.

Summary

A series of experiments using rats has shown that in the presence of sufficiently high dosages of dinitro-*o*-cresol to cause characteristic D.N.C.-poisoning five of the six barbiturates tested were significantly potentiated in the rapidity of onset, depth, and duration of their narcotic effects.

The action of the two thiobarbiturates tested—thiopentone and thialbarbitone—was potentiated so that normally non-fatal anaesthetizing doses led to almost immediate cyanosis and death. Of the oxygen barbiturates, pentobarbitone, amylobarbitone, and phenobarbitone were markedly potentiated by D.N.C., but hexobarbitone did not appear to be significantly influenced.

Barbiturate potentiation by D.N.C. appeared to require the presence of high D.N.C. dosages. Low dosages, causing no obvious D.N.C.-poisoning, did not appear to increase barbiturate narcosis.

It is strongly recommended that barbiturate drugs, especially thiobarbiturates, should not be used for the induction of surgical anaesthesia in a person suffering from D.N.C.-poisoning, and that barbiturate sedation in such cases should be carried out with comparatively small dosages, in anticipation of a possibly enhanced effect due to the synergistic action of D.N.C. and the barbiturates on cellular respiration.

We are grateful to Dr. J. M. Barnes for drawing our attention to this subject, and for advice during the investigation.

REFERENCES

Bain, J. A. (1952). *Fed. Proc.*, **11**, 653.
Bidstrup, P. L., and Payne, D. J. H. (1951). *British Medical Journal*, **2**, 16.
B.M.A. (1951). Circular letter to practitioners, March.
Brody, T. M., and Bain, J. A. (1954). *J. Pharmacol.*, **110**, 148.
Edson, E. F. (1955). *British Medical Journal*, **1**, 841.
Martindale (1952). *Extra Pharmacopoeia*, 23rd ed., **1**, 1020. London.
Pollard, A. B., and Filbee, J. F. (1951). *Lancet*, **2**, 618.

Blood donations to hospitals in England and Wales through the National Blood Transfusion Service in 1954 were more than ever before: 700,202, compared with 659,674 in 1953 and 669,000 in 1944, the year in which D Day fell. Last year 104,161 people gave their blood for the first time, and by the end of December the total strength of the donors' panel was 540,389, an increase of nearly 25,000 compared with 1953. To ensure that no one need be asked to give blood more than twice a year the National Blood Transfusion Service needs 650,000 regular donors.

Medical Memorandum

Thrombocytopenic Purpura during Chloramphenicol Therapy

Much has been written about the occurrence of blood dyscrasias during chloramphenicol therapy. Aplastic anaemia is the commonest finding, but agranulocytosis also occurs. Hodgkinson (1954) collected 31 cases of poisoning by chloramphenicol; 28 were cases of aplastic anaemia, while three had granulocytopenia with a normal erythrocyte count. He recommended that the maximum dosage of chloramphenicol administered to a child should be 100 mg. per kg. body weight daily for seven days.

Purpura has frequently been the first sign of a toxic reaction. In all reported cases such a purpura has been shown to be a manifestation of aplastic anaemia. Often the platelets have been greatly reduced: Wilson *et al.* (1952) recorded 9,000 platelets per c.mm., but such low figures have always been accompanied by a fall in both erythrocytes and granulocytes. A slight fall in platelets has been reported accompanying granulocytopenia without anaemia (Hodgkinson, 1954), but there seems to be no previous record of thrombocytopenic purpura as the sole manifestation of chloramphenicol poisoning.

Case Report

A boy aged 5 was seen by his doctor on account of cough. A week after the onset of the disease whooping and vomiting began, and he coughed up a little blood. His doctor made a diagnosis of whooping-cough, and prescribed chloramphenicol palmitate, 60 minims (3.6 ml.) t.d.s. When he had received a total of 2 fl. oz. (57 ml.) of this (2 g. of chloramphenicol) he developed a widespread purpura. He was then admitted to Plaistow Hospital, a fortnight after the onset of his cough.

On admission there were ecchymoses on the limbs, trunk, palate, and alveoli, and inside the right cheek. He also had bilateral subconjunctival haemorrhages. The lungs showed no abnormal physical signs. There was a slight tachycardia, with occasional extrasystoles. The spleen and liver were not palpable. The temperature was 101.2° F. (38.4° C.). The haemoglobin was 95%. The white blood cells numbered 13,500 per c.mm. (32% polymorphs, 64% lymphocytes, and 4% monocytes). The platelets numbered 5,000 per c.mm., and the bleeding-time exceeded ten minutes.

Treatment with chloramphenicol was discontinued, and crystalline penicillin, 500,000 units, was injected eight-hourly. The platelets rapidly rose in number. On the day following admission there were 83,000 platelets per c.mm., and only a few fresh purpuric spots were found. On the 13th day after admission the platelets numbered 203,000 per c.mm., and the purpuric lesions had all healed. The cough also had disappeared. On the 20th day the platelets numbered 230,000 per c.mm. The liver and spleen were not palpable at any stage. The patient was then discharged, the white blood cells numbering 14,800 per c.mm. (40% polymorphs, 60% lymphocytes).

Comment

The interest of this case arises from two facts. Firstly, a severe but transient thrombocytopenia occurred during treatment with chloramphenicol, with no fall in the haemoglobin or granulocytes. Secondly, this toxic manifestation occurred after only 2 g. of chloramphenicol had been given to a child of 5 years, spread over five days. This is about a seventh of the maximum dosage recommended by Hodgkinson (1954).

My thanks are due to Dr. R. W. Tannahill, physician in infectious diseases to Plaistow Hospital, for permission to publish this case.

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REFERENCES

Hodgkinson, R. (1954). *Lancet*, **1**, 285.
Wilson, L. E., Harris, M. S., Henstell, H. H., Witherbee, O. O., and Kahn, J. (1952). *J. Amer. med. Ass.*, **149**, 231.

Reviews

HIGH-ENERGY RADIATION

Radiation Biology. Volume I, High Energy Radiation. Parts I and II. Edited by Alexander Hollaender with the co-operation of Austin M. Brues, Berwind P. Kaufmann, Hermann J. Muller, and Lauriston S. Taylor. (Part I: Pp. 1–626; Part II: Pp. 627–1265. Illustrated. £7.) London, New York, Toronto: McGraw-Hill Book Company Inc. 1954.

These two substantial books constitute the first volume of a series of three comprehensive works on the biological effects of radiations and deal with ionizing radiations. It is intended that ultraviolet radiation and visible light will be considered in the other two volumes. In the preface the editor explains that these volumes grew out of a tentative plan to revise the two-volume work *Biological Effects of Radiation* edited by B. M. Duggar and published in 1936. However, there was so much new work to be included that the only practicable plan was to bring out a new series of books.

The present volumes are encyclopaedic and deal with a considerable number of topics in the field of radiobiology. The eighteen chapters are essentially monographs by people who have devoted most of their working lives to their special subjects. The chapter by U. Fano is a useful introduction to the principles of radiological physics, and that by L. D. Marinelli and L. S. Taylor is a very clear account of the measurement of ionizing radiations for biological purposes. Chapter 3, by James Franck and Robert Platzman, is an excellent survey of the physical principles underlying radiation-chemical and radiobiological reactions. The only English contribution is by Walter M. Dale, of the Christie Hospital and Holt Radium Institute, Manchester. His rather short chapter entitled "Basic Radiation Biochemistry" summarizes a field in which he has carried out pioneer work and is extremely good. The chapter by Raymond E. Zirkle on "The Radiobiological Importance of Linear Energy Transfer" is an important contribution, and Table 6–1 is a useful summary of the relations between linear energy transfer of various radiations and their relative biological effectiveness for different types of response. The last two chapters of Part I are by H. J. Muller and deal with genetic effects produced by radiation. They are not easy reading, but in the opinion of the reviewer constitute the best account of this subject which has appeared in recent years.

The first two chapters of Part II deal with chromosome aberrations produced by ionizing radiations in animal and plant cells, and provide a valuable account of an important aspect of the biological action of ionizing radiations which has not yet been sufficiently assimilated into current thought about therapeutic applications. The next chapter, on immediate effects on division, morphology, and viability of the cell, introduces a considerable amount of new information in a field rather more familiar to medical workers. An outstanding chapter is that on genetic effects of radiation in mammals by W. L. Russell, which should be studied by everyone interested in this field. The work described in the next chapter, by Mrs. Russell, on the effects of radiation on mammalian prenatal development, requires serious consideration at least from the point of view of diagnostic radiology. The pathological physiology of radiation injury in the mammal is discussed at length by Harvey M. Patt and Austin M. Brues and is a useful and critical contribution. Haematological effects of ionizing radiations are considered by Leon O. Jacobson, and histological changes after irradiation by William Bloom. The final chapter, on carcinogenesis by ionizing radiations by Jacob Furth and the late Egon Lorenz, is a useful review of this important subject.

The references are given in lists at the end of each chapter and include the relevant European literature, which is often of importance. The name index and subject index for the complete volume are given at the end of Part II and appear to be very good.

It is a sign of the times that the main interest in the biological actions of ionizing radiations is no longer the therapeutic use of radiations in medicine. The difference in the points of view between these volumes and Lazarus's *Handbuch der gesamten Strahlenheilkunde,* published in 1928, is striking. The increase in knowledge of radiobiology since 1936 has as yet had little influence on practical radiotherapy. It is the opinion of the reviewer that the time is now approaching when radiobiology will make a contribution to clinical radiotherapy comparable with that achieved by the application of physics. Despite the rather high price, the volume under consideration should become a standard book of reference for all those interested in the advancement of radiotherapy, as well as for those who are working in the various scientific aspects of radiobiology.

J. S. MITCHELL.

ENDOCRINOLOGY AND PSYCHIATRY

Endokrinologische Psychiatrie. By M. Bleuler. (Pp. 498 + xii; illustrated. D.M. 46.50.) Stuttgart: Georg Thieme Verlag. 1955.

Whenever a visitor with endocrinological interests is invited to the chronic wards of a mental hospital he seems amazed at the number of apparent endocrine abnormalities visible in psychiatric patients. But when this first, purely physiognomic impression is put to the test, and organs and body fluids and excretions are examined, very little definite remains. Minor variations, often within the range of the normal, are present, but nothing is found that could contribute to the symptomatology of the mental disease or to its aetiology. There seems to be an obvious interrelation between psychic and endocrine functions, but its nature is still problematic and knowledge about it inconclusive.

This experience of hope and disappointment must have struck many psychiatrists and endocrinologists. It is repeated and well demonstrated in this book, in form and size a textbook, which courageously attempts to represent the border territory between the two relatively young branches of medicine. The aim was, according to the author, to describe the psychopathology of endocrine diseases and the endocrinological pathology of mental illness. While there is a limited knowledge of psychological symptoms in endocrine illness and abnormality, the second aim is much more difficult to fulfil: the question whether minor and major mental symptoms have any endocrine pathology to which they can be related is highly debatable. However, the general idea of connexion between endocrine and psychic functions is worth studying, and also the practical approach of ascertaining how far endocrine diseases can be successfully treated by psychotherapy, and mental diseases by endocrine preparations and procedures such as operative interference with organs.

Bleuler discusses all this with great thoroughness. But, while he is, if anything, too modest when reporting on the relatively meagre results of his own studies and those of his pupils, he shows little of his critical abilities in quoting from the works of others, and he does not use the right of selection which an expert of his standing can be expected to do. What starts as a textbook becomes, over large sections, a review of the literature through which the reader has to wade with little support from the author, and with little positive result. Most of the writings naturally concern themselves with the darker problems of endocrine pathology and therapy in mental illness, where verbosity and hypotheses often replace factual observation. The present text has not entirely escaped this danger of wordiness. However, with its list of almost 3,000 references, its full index of names and of subjects, which altogether take up more than 100 of 400 pages, the volume fulfils the demand for a reliable book of reference and will prove indispensable for all workers in the field. Bleuler's call for new techniques in the laboratory, and for psychiatrists who have time to devote themselves to these studies in the laboratory and combine them with the clinical and humane approach to their patients, will find the consent of everybody concerned.

W. MAYER-GROSS.

DERMATOLOGY IN THE U.S.A.

Diseases of the Skin. By Oliver S. Ormsby, M.D., and Hamilton Montgomery, M.D., M.S. Eighth edition. (Pp. 1,503; illustrated. £8.) London: Henry Kimpton. 1954.

This encyclopaedic work has become a necessary book of reference for every dermatologist, but its increasing weight would now seem to make two volumes desirable. The revised edition was completed and in proof when Dr. Ormsby died, and the work is a testimony to his considerable contribution to dermatology over the course of many years. Much has been rewritten and brought into line with the rapid advances being made in medicine, and some sections, as physiology, vascular disorders, and mycology, have been put into the hands of experts in special fields. There are many new illustrations, which are good, as is the whole production.

Particular mention may be made of the excellent chapters on physiology, including the new contributions to the problem of pigmentation, sweating, and innervation. There is some rearrangement of the sections to bring the material into line with modern concepts. The clinical descriptions of the major ills naturally stand, though treatment is often revised and much of the old vague general measures has properly been deleted.

There is little that the British dermatologist will not accept, making occasional allowances for a different country with a different climate and some variation of endemic infection. The authors do not agree with the modern view that parapsoriasis, like poikilodermia, may develop into one of the malignant reticuloses, and they retain pityriasis lichenoides chronica as a variety of parapsoriasis. Chrysarobin is still quoted as the treatment for psoriasis, and no mention is made of dithranol; few in this country would agree with the commendation of *x*-ray therapy for this disease. Dysidrosis still claims a section, and Nestorowsky's work in 1906 is quoted as "a recent study." Podophyllin resin is not mentioned in the treatment of lichen simplex.

Indeed, viewed from the point of view of the general practitioner, treatment as a whole is not a strong feature in this work, especially in the common diseases. It is noted that the use of vaccines has largely been abandoned in dermatology. Attention is drawn to the work of British dermatologists on the histology of pemphigus and pemphigoid, though the treatment of dermatitis herpetiformis does not entirely reflect modern practice in this country. To say that the treatment of nodular panniculitis is symptomatic is not entirely clear, and experience to-day would not support the suggestion that anthrax is frequently fatal.

But these are small details mentioned only for attention in the next edition. The work as a whole is excellent and a reflection of the very high place, and indeed the leadership, enjoyed by the United States in this field of medicine.

J. T. INGRAM.

AUSCULTATION AND PERCUSSION

Lehrbuch der Auskultation und Perkussion. By K. Holldack. Foreword by Professor Dr. Med. Curt Oehme. (Pp. 195+xi; illustrated. D.M.27.) Stuttgart: Georg Thieme Verlag. 1955.

The author of this textbook of auscultation and percussion rightly stresses these ancient and important arts, which in these days of elaborate chemical and instrumental examination may easily become neglected. It is perhaps a little curious that these two topics are named in the order of the title, for historically and in usual clinical procedure they are reversed. However, in the book the order of clinical ritual seems to be inspection—and that very rightly always should come first—then percussion, thirdly auscultation, and last palpation. This is different from our clinical practice here.

In the next large section the author considers the inspection of the head, or rather of everything that may be noted above the collar. This opens up a wide field, all clinical medicine almost. One might suggest that such a method might well be applied to the hands. The neck is considered in the same way. Such a regional procedure has certain advantages; in practice something of the sort is usually adopted, even if it is a little difficult for the student at first. In dealing with the thorax the order of procedure is the usual; but here there is the likelihood of confusion, for the lungs and heart are not taken separately, which is really easier for the beginner. Later he can integrate. It seems odd to find that the percussion hammer and pleximeter are still recommended. The sections on auscultation are illustrated by clear diagrams and phonocardiograms, and there are plenty of diagrams to show physical signs. The central nervous system hardly comes into all this. In the examination of the abdomen a curious technique is advocated for examining the liver edge between finger and thumb. I believe it was Osler who said that a specialist in a case of obscure abdominal disease examined the testes and put a finger in the rectum. These procedures are rather neglected in this book. Nevertheless an attempt is made to present the old enlightened by the new.

TERENCE EAST.

CONSCIOUSNESS

Brain Mechanisms and Consciousness. A Symposium organized by the Council for International Organizations of Medical Sciences. Editor for the Council: J. F. Delafresnaye. Consulting Editors: Edgar D. Adrian, Frederic Bremer, and Herbert H. Jasper. (Pp. 556+xv; illustrated. 42s.) Oxford: Blackwell Scientific Publications. 1954.

There are those who think that the habit of symposia (or, at any rate, their publication) is somewhat overdone. This may well be so, but it cannot be denied that the published reports often make useful and entertaining reading—useful in so far as some participants take the opportunity to present a brief but authoritative review of recent advances in their subject, and entertaining in so far as others permit a glimpse of the working of their own minds by speculating far ahead of their current investigations.

By their very nature, reports of symposia do not allow a ready assessment of their contents in a short review, for the standard of the contributions shows such wide variations, and the present volume is no exception in this respect. The title excites attention by its ambitious implications, and most of the contributions are devoted to attempts to analyse the anatomical and physiological correlates of conscious processes. The net result of the discussions does not, of course, explain "consciousness" in terms of neural activities—indeed, it is difficult to imagine that such an explanation ever will be found. On the other hand, we are beginning to learn more about the negative aspect of the problem by defining those mechanisms upon the integrity of which conscious awareness seems to depend. Much attention in the symposium has been given to the so-called "centrencephalic system," a term which is not without disadvantages, of which perhaps the most serious is that it seems premature to attempt thus to circumscribe a formation whose very nature is its diffuseness both anatomically and physiologically. There is undoubtedly good evidence that the sort of cortical activity which appears normally to be associated with conscious processes in man is conditioned by certain brain-stem mechanisms. But then it is also conditioned by quite a lot of other things as well, and it seems important at this stage of the inquiry to resist the facile interpretation that consciousness is a function of the "centrencephalic system" itself.

Not the least interesting part of this book are the reports of the discussions following the contributions. These discussions make it clear that the several attempts to define "consciousness," so that this phenomenon can be brought into some context with physiological reasoning, have so far been unsuccessful. They also make it clear that opinions vary widely on the functional significance of the electrical responses derived from stimulating the diffuse reticular formations of the brain-stem.

W. E. LE GROS CLARK.

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THE ANNUAL MEETING

In the last two issues of the *Journal* we have recorded some of the events—scientific, social, ceremonial—that took place in Toronto during the Joint Annual Meeting of the British Medical Association, the Canadian Medical Association, and the Ontario Medical Association. All told, just on five thousand persons registered, including the wives of delegates, and representatives of the Press and the pharmaceutical industry. This was a record attendance for a medical convention to be held on Canadian soil, and those British visitors who had the great good fortune to be in Toronto in the second half of June will long remember the friendly warmth and feeling of our Canadian hosts; the exemplary efficiency of the organization and the thoughtfulness behind it; and the intellectual stimulus that came from meeting Canadian doctors in scientific session and in those informal talks that are so valuable a feature of medical and scientific conventions. Many, too, had the opportunity of visiting some of Toronto's well-equipped hospitals and such famous institutions as the Charles H. Best Institute and the Connaught Research Laboratories, from which have come fundamental contributions in the preparation of the Salk vaccine against poliomyelitis. Driving along the straight thoroughfares of Toronto, passing the sturdy Parliament building and the lovely campus of the university into the countryside beyond, the visitor could not fail to be impressed by the vigour and self-confident optimism of the stalwart Canadian character, responding freely to the challenge of the opportunities now abounding in the ten Provinces of the great Dominion. And the visitor would surely be pardoned by the other nine Provinces if he concluded that Ontario in general, and Toronto in particular, was the heart of Canada, for here he was at an Annual Meeting larger than any held in Britain yet suffused throughout with an effortless friendliness.

To the many individuals and committees responsible for this outstanding success we in Britain are deeply indebted—to Dr. Arthur Kelly, the general secretary of the Canadian Medical Association, and his assistant, Dr. Arthur Peart; to Dr. Glenn Sawyer, secretary of the Ontario Medical Association, and his assistant, Mr. A. K. Gillies; and to Drs. B. V. Bradley, R. W. I. Urquhart, C. D. Gossage, and F. R. Griffin for the hard work done by them and their committees. The meeting, too, must have owed much to the support and publicity given it by the *Canadian Medical Association Journal* under its recently retired Editor, Dr. H. E. MacDermot, and his successor, Dr. S. S. B. Gilder, the latter also taking an active part in the work of public relations. An institution, Emerson said, is the lengthened shadow of one man, and so in a special sense is a convention. The convention in Toronto—to continue to use this convenient North American designation—took its tone and atmosphere from the genial personality of the new President of the British and Canadian Medical Associations, Dr. T. C. Routley. With his gracious wife Dr. Routley seemed to be able to be present at all the occasions, small and great, that go to compose an Annual Meeting, both of them ready with deep friendliness and kindness to make everyone welcome and at home. Seldom can the ladies at an Annual Meeting have had such a right royal time under such beneficent guidance as Mrs. Routley provided. To its new President and his lady the B.M.A. is profoundly grateful.

The Toronto meeting, for the B.M.A., was in effect the second half of its annual gathering, the first, the business half, having been completed in London early in June. The second half is devoted to the work of the scientific sections, a yearly reminder of the real nature of the doctor's task in life. Dr. R. F. Farquharson, chairman of the Programme Committee of the C.M.A., had, with his British colleagues, provided an attractive bill of fare to meet the varying tastes of approximately 4,000 medical men and women. What was particularly noticeable to the British doctor was the unflagging interest of the Canadian doctor in the scientific side of the meeting, especially in the round-table conferences, which are described in an annotation at p. 112. These conferences are something we might imitate in Britain, though to have round-table conferences alongside several plenary and general sessions and numerous section meetings means almost an excess of good things. But seldom at an Annual Meeting of the B.M.A. can there have been such a consistently high level of attendance at so many sessions, a tribute indeed to those who planned the programme. The scientific exhibition showed that our confrères on the other side of the Atlantic are very much alive to techniques of display and visual education, and the Medical Exhibitors Association of Canada put on a most instructive display of drugs, books, periodicals, instruments, and equipment. Nor must we forget a most enlivening collection of paintings by Canadian doctors that in some touched the level of professional excellence.

And so the many parts came together in a unity made complete by the presence of doctors from eleven countries of the British Commonwealth of Nations, all speaking the same language, owning to a common allegiance, and sharing a common belief in the tenets of a free society. It was appropriate, too, that many colleagues from the U.S.A. and officials of the American Medical Association should take part in this English-speaking union of medical men and women. Old friendships cemented, new friendships made, a deeper understanding of each other's problems, a phrase in a speech or conversation that acts as a spark to the imagination, contact with fresh minds and new ideas, all the ferment of lively communication—these are what in their different ways nearly 4,000 doctors experienced in Toronto. And their indebtedness is great to all those who made this experience possible, and especially to the President of the B.M.A. for 1955–6, Dr. T. C. Routley.

RETROLENTAL FIBROPLASIA

Since retrolental fibroplasia was first described in 1942 by T. L. Terry, of Boston,[1] much work has been done to clarify the aetiology, the pathological changes, and the clinical appearances of this distressing disease. The essential change is an angioblastic proliferation of the blood vessels in the retina of a premature baby. The early changes are reversible in many cases, but the disease may progress to a cicatricial stage causing partial or complete blindness. The earliest clinical studies showed an apparent association between the development of retinal changes and administration of oxygen,[2 3] and a gratifying fall in the incidence of the disease followed a reduction in the administration of oxygen to premature babies.[4] Elegant experiments performed in Britain by N. Ashton and his colleagues[5] and by other workers abroad[6 7] showed that changes resembling retrolental fibroplasia could be produced in newborn kittens and other animals if they were subjected to a high concentration of oxygen.

This week in the *Journal* appears a report of an inquiry made by Drs. J. T. Boyd and K. M. Hirst (p. 83) on behalf of the Ministry of Health into the incidence and distribution of retrolental fibroplasia among premature infants born in England and Wales in 1951. The report concerns 6,926 infants who had weighed less than 4 lb. 6 oz. (2 kg.) at birth and who had survived for at least two months. The most interesting fact to emerge from this survey is that all of the 127 cases discovered were in infants born in hospital or transferred there soon after birth, while there were none in infants who remained at home. This suggests that some factor in the hospital care of premature babies predisposes to retrolental fibroplasia, and further evidence that it is the administration of oxygen comes from the work of a conference initiated in 1952 by the Medical Research Council, whose report we also publish this week (p. 78). The conference considered information relating to 1,095 premature babies cared for in seventeen different units over a period of twenty months. Much of its report concerns the administration of oxygen, though other factors that might be concerned in the aetiology of the disease were also considered. Some association was found between maternal bleeding during pregnancy and the subsequent development of retrolental fibroplasia in the baby, and also a possible connexion with neonatal anoxia. The significance of the latter finding is difficult to evaluate, for the anoxic baby is the one most likely to be given oxygen; but many babies who were not clinically anoxic developed retrolental fibroplasia. The parts played by anoxia on the one hand and oxygen administration on the other in the development of the disease are not yet clear, but each may possibly exert its effect at a different stage in the development of the retina. The association with anoxia may explain the few cases of retrolental fibroplasia which have occurred when no oxygen has been given. In the Medical Research Council survey none of the 344 babies who were not given oxygen developed the disease. Only two out of 515 who were given oxygen for less than five days showed any pathological retinal changes, but thereafter the incidence of the disease rose steeply with duration of treatment, until three out of every five babies given oxygen for thirty-one days or more were affected.

Now that the dangers of oxygen therapy have become much clearer, the indications for its use must be studied with care. Ten years ago it was common practice to keep a small premature baby in an oxygen-enriched atmosphere for three or four weeks, even though it showed no cyanosis when in atmospheric air. Certain features peculiar to premature infants were held to justify this. The pulmonary alveoli in the premature lung are incompletely developed and maintain a thicker barrier than normal between the blood stream and the alveolar air. Cyanotic attacks are frequent in premature infants. An irregular respiratory rhythm is common and there

[1] Terry, T. L., *Amer. J. Ophthal.*, 1942, **25**, 203.
[2] Campbell, K., *Med. J. Aust.*, 1951, **2**, 48.
[3] Ryan, H., *Amer. J. Ophthal.*, 1952, **35**, 329.
[4] Jefferson, E., *Arch. Dis. Childh.*, 1952, **27**, 329.
[5] Ashton, N., *et al.*, *Brit. J. Ophthal.*, 1954, **38**, 397.
[6] Gyllensten, L. J., and Hellström, B. E., *Acta paediat.* (*Uppsala*), 1952, **41**, 577.
[7] Patz, A., *et al.*, *Amer. J. Ophthal.*, 1953, **36**, 1511.
[8] Wilson, J. L., *et al.*, *Amer. J. Dis. Child.*, 1942, **63**, 1080.
[9] Smith, C. A., and Kaplan, E., ibid, 1942, **54**, 843.
[10] Reardon, H. S., *et al.*, ibid., 1950, **79**, 372.
[11] Russell, P. M., *M.D. Thesis*, Univ. of Liverpool, 1955.
[12] Lanman, J. T. *et al.*, *J. Amer. Med. Ass.*, 1954, **155**, 223
[13] Patz, A., *Amer. J. Ophthal.*, 1954, **38**, 291.
[14] Kerr, J. D., and Scott, G. I., *Arch. Dis. Childh.*, 1954, **29**, 543.

is evidence that this is due to anoxia and may be abolished by the administration of oxygen.[8] Against that the newborn infant has a greater tolerance for anoxia than has the adult, and it is possible that a state of relative anoxia may be normal and quite unharmful for the premature baby. Several workers[9 10] have shown the oxygen saturation of arterial blood in premature babies to be slightly lower and subject to greater fluctuatioh than in those born at term, and in a recent study[11] no correlation was found between oxygen saturation of blood and the clinical state and progress of premature infants. All will agree that oxygen may be essential in the treatment of asphyxia immediately after birth. It should also be given to any premature infant who subsequently shows cyanosis, provided that other aspects of treatment such as the maintenance of a clear airway are not neglected. When an infant has some pulmonary atelectasis with respiratory embarrassment it is probably more important to provide an atmosphere with a high relative humidity than with a high oxygen content, and the addition of an aerosol may also help.

Already the use of oxygen has been greatly curtailed in many premature-baby units, and the clinical and experimental data now available justify that change of practice. Administration of oxygen, except for emergency use, should require a specific medical order. The concentration to be attained should be specified rather than the rate of flow. J. T. Lanman and his colleagues in New York[12] found a higher incidence of retinal changes in infants given a high (average 69%) concentration than in those nursed in a lower one (average 38%), and a similar experience was recorded by A. Patz.[13] But a fairly low concentration of oxygen is not a guarantee of safety, and the duration of therapy is probably of prime importance. This is emphasized in the Medical Research Council report and was also the experience of J. D. Kerr and G. I. Scott.[14] Perhaps when any premature baby is receiving oxygen a number of red labels should be fixed to the cot or incubator, one representing each day that a potentially dangerous form of treatment has been continued.

INFECTIONS IN THE NEWBORN

To-day an increasing number of babies are born in hospital, and this has obvious advantages, particularly for the mother. On the other hand, reports are appearing more frequently of hospital infection among the newborn infants. In the main these are cases of minor staphylococcal lesions of the eyes and skin, and in common with other hospital infections due to this organism are often caused by strains resistant to the antibiotics in common use. Other cases are those in which the cord stump becomes infected, and from these a wide range of organisms may be isolated. Most of the infections are very trivial, and the incidence in any institution will often reflect the enthusiasm with which they are reported rather than the true number of babies affected. Nevertheless, there are a few babies who are seriously ill, and even a mildly inflamed eye may lead to an infant and its mother remaining a day or two longer in hospital. Capon,[1] in a recent article in this *Journal*, mentions two possible causes of infection. The first is a diminution in babies' immunity, leading to an increased susceptibility, though the ease with which the majority of minor infections are thrown off does not support this view. The other cause, which he favours, is overcrowding in nurseries and overwork of nursing staff associated with the high staphylococcal carrier rate found among hospital workers. That this is the causal factor is confirmed by Pickerill,[2] in New Zealand, who has shown that hospital infection is almost eliminated when mothers can nurse their babies in separate rooms of their own. Since it would be quite impracticable for all maternity patients to nurse their babies away from all other patients and out of contact with hospital staff except by having all confinements in the home, hospitals must therefore direct their efforts to reducing the chances of babies' becoming infected in other ways.

The methods by which organisms are transferred from patient to patient and from staff to patient are now fairly well understood and have recently been reviewed by Lowbury.[3] Methods of control, however, are not so clear. Organisms can reach a baby from cot bedding, and other materials which are directly in contact with it, and from dust in the nursery. But the commonest sources of staphylococcal infections, both trivial and serious, are the hands of the attendants and the droplets from their noses, though ward and nursery dust may well provide a reservoir of organisms. A number of measures are now being tried to reduce this transfer of staphylococci from staff to patient. In burns units and the like the control of dust by oiled floors and blankets has been described, and the use of filtered air for dressing-theatres introduced by Colebrook[4] could possibly be applied to nurseries. But the most promising approach to this problem is to prevent the transfer of organisms from staff to baby, for anything which will interfere with this transfer will

[1] *British Medical Journal*, 1955, 1, 803.
[2] *Lancet*, 1954, 1, 425.
[3] *British Medical Journal*, 1955, 1, 985.
[4] *Lancet*, 1946, 1, 561.
[5] Murray, J., and Calman, R. M., *British Medical Journal*, 1955, 1, 81.
[6] Gould, J. C., and Allan, W. S. A., *Lancet*, 1954, 2, 988.

reduce the incidence of infection. At Queen Charlotte's Hospital an antiseptic hand-cream has been used to suppress organisms transferred to the nurse's hand from her nose, and the results obtained suggest that this has some value.[5] As the site at which carriers most commonly harbour staphylococci is in the nose, the use of antibacterial nasal drops or cream has been advocated.[6] Any preparation distributed to healthy nurses must be acceptable to the staff concerned, and it is difficult to find drops sufficiently free from smarting, irritation, or unpleasant taste to ensure their proper use. Attempts to use antibiotics for this purpose are dangerous owing to the almost inevitable emergence of resistant strains, and the use of drugs of this type, which may be required for systemic treatment, should be avoided. It often happens that staphylococci are again recovered from carriers after a short interval of freedom, but a reduction in the total number harbouring the organisms can usually be achieved by treatment. An ideal agent for this purpose has not yet been found, but a combination of nasal drops and a hand-cream may well produce a reduction of clinical infections.

Severely infected babies must be isolated, but it is perhaps too much to hope with Professor Capon that all babies with slightly infected eyes can be completely isolated immediately. Little is yet known about the complex incubators now coming into use in maternity hospitals; and the problems involved when a severely infected baby has been nursed in one are by no means solved, though some attempt is made to remove infected dust and fluff and to sterilize the humidifier and other parts of the air circulator.

A baby is born without organisms in its conjunctiva, nose, mouth, or alimentary tract unless the membranes have been ruptured for some considerable time. During the first day or two of life all these sites become colonized by organisms of one sort or another, and it is disturbances of this natural process which appear as infections. But what is not understood is why of two babies handled by the same staff in adjacent cots one will develop a local staphylococcal lesion and the other will not. Perhaps natural immunity comes into play or perhaps a detail of handling is the determining feature. The fact that there are antistaphylococcal lysins in the blood does not necessarily prevent the occurrence of local staphylococcal infections, and it is possible that the presence of some immunity may only confine the lesion to one particular site. On the other hand, as with staphylococcal and other infections in adults, the differences in the susceptibility of infants may lie in the fields of metabolism and endocrinology.

ROUND-TABLE CONFERENCE

Although a well-established form of meeting across the Atlantic, the round-table conference was a novelty to many British visitors to the Joint Meeting at Toronto. From 9 a.m. to 10.15 a.m. each morning there was a choice of four such conferences on subjects which ranged from low backache to the management of coronary thrombosis. A brief report of one of the conferences—that on poliomyelitis—appears on another page. At the table are seated four to eight people centred round a chairman, and the procedure resembles that of a radio or television discussion group. The atmosphere is informal and the impression is one of unrehearsed discussion, unhampered by the confines of a script and open to the intrusion of aphorism and wit. But, just as the "best impromptu speeches are the most carefully rehearsed," so behind the apparent informality lies a certain amount of preparation, although not of rehearsal.

Some three or four months before the convention is scheduled, and after the constitution of the panel has been decided, the chairman prepares a list of questions designed to cover the chosen subject comprehensively, with particular emphasis on the practical and clinical aspects. This list is circulated among the panel, it being indicated who is to be called on to answer which question. At the same time suggestions for alterations or modifications in the questions are solicited. The panel are warned that five minutes is the maximum time allowed for any one reply, and the rigid enforcement of this rule prevents a slowing down of the tempo. The preparation is therefore limited, and the success of the conference depends more than anything else on the personality and the adroitness of the chairman. Invidious though it may be to single out one chairman for mention, Dr. Elinor Black (Winnipeg), at the conference on prenatal care, gave a perfect exhibition of the qualities required. She was obviously familiar with the views of her panel, for she was able to draw out contrasting opinions on the same subject. The discussion was kept fluid and any tendency to prolixity was neatly headed off. More humour was injected than is usually shown at scientific meetings, and the audience was kept alert and attentive. The final fifteen minutes of the session are devoted to questions from the audience. In the interests of audibility and smooth running of the meeting these questions are not asked from the floor but are handed up to the chairman in written form.

The round-table conferences are attractive partly because the ear is more attentive and the mind more alert to diversity than to monotony. The rapid fire of a lively panel discussion is more assimilable than the prolonged development of a theme in a single paper. These meetings, on topics of great interest to the general practitioner, were among the most popular, enjoyable, and instructive of the whole convention. Something like them might well find favour at future B.M.A. Annual Meetings.

GENETIC EFFECTS OF RADIATION IN MAN

At present there are two lines of evidence on which to base an estimate of the number of mutations produced by a particular dose of ionizing radiation in man. The first is by analogy from animal experiments, the second is by the study of children born to men and women who have been exposed to an unusual dose of radiation. Unfortunately animal experiments on a large enough scale to give reliable results have been made on organisms very unlike man, such as the fruit-fly,[1] and it is doubtful how far these results apply to our own species. The only mammal on which the effects have been systematically studied is the mouse[2]; here the results are sufficient only to suggest that ionizing radiations are more effectual in inducing mutations than they are in the fruit-fly.

Two attempts have been made to measure directly the effects on man himself—on survivors of the atomic bombs in Hiroshima and Nagasaki, and on radiologists in the United States of America. Only a preliminary report of the Japanese study is available,[3] covering some 2,000 births. No strong indication was found of any effect on the sex ratio, the malformation rate, the stillbirth rate, or the birth weights of the children of whom at least one parent had developed one or more of the cardinal symptoms of radiation injury in the months after the bombing. The survey on American radiologists[4] was made by a routine postal questionary to over 3,500 of them, and the same questionary was sent to a similar number of physicians in other specialties. As so often happens with postal questionaries, the replies were far from complete. About three-quarters of the radiologists, but only about half of the other physicians, responded. No significant difference in the number of foetal deaths in the two groups was found, but there was a small and significant increase in the number of congenital malformations among the children of the radiologists (5.99% of 5,461 children born to radiologists, as compared with 4.84% of 4,484 children born to the controls). But there is ample room for bias in the incomplete response to the questionary, and it cannot be assumed that this small difference is due to irradiation.

The authors of both surveys are nevertheless careful to make the point that their inconclusive results should not be interpreted as indicating that the genetic effects of radiation in man are small. Animal experiments have shown that the great majority of mutations, whether occurring naturally or following artificial radiation, are at least partially recessive and so unlikely to be detected in the first generation after exposure. Perhaps the effects most likely to be detected in the first generation are not stillbirths and congenital malformations, but a reduction in adult body size and in average length of life. These would require a longer follow-up for their detection.

[1] Muller, H. J., in *Radiation Biology*, edited by A. Hollaender, New York, 1954, Vol. I, Part 1, p. 351.
[2] Russell, W. L., in *Radiation Biology*, edited by A. Hollaender, New York, 1954, Vol. I, Part 2, p. 825.
[3] Neel, J. V., *et al.*, *Science*, 1953, **118**, 537.
[4] Macht, S. H., and Lawrence, P. S., *Amer. J. Roentgenol.*, 1955, **73**, 442.

HYPERNATRAEMIA

While sodium depletion with low concentration of sodium in the plasma is a fairly common complication of some diseases in which the gastro-intestinal secretions are lost or renal conservation of sodium is impaired, hypernatraemia is far more rarely encountered. It is surprising therefore to read that H. M. Schoolman, A. Dubin, and W. S. Hoffman[1] have seen over 100 cases in the last four years in one hospital in the United States. Thirty-three of their cases were what they describe as the primary desiccation syndrome—that is, loss of water in excess of loss of sodium. Of these, 15 were infants under the age of 2 with mild diarrhoea and fever, and 18 were adults, many of them senile, in whom hypernatraemia developed as a complication of fever, hot weather, and inability to look after themselves. The prognosis in these cases was good and they responded rapidly to oral or parenteral administration of water. The smallest group of nine patients developed hypernatraemia as a complication of the treatment of diabetic acidosis with insulin and salt solutions alone. They responded well to treatment with water, the plasma sodium falling to normal within 24–48 hours. The largest group of cases consisted of 80 patients with some kind of intracranial lesion such as meningitis, cerebral metastases, encephalomalacia, or subarachnoid haemorrhage. Reduction of plasma sodium concentration to normal was difficult, and most of the patients died with hyperpyrexia even when treatment of the hypernatraemia was successful.

Although hypernatraemia may occur as a complication of gastric[2] or oesophageal haemorrhage,[3] untreated severe dehydration,[4 5] acute toxic renal damage,[6 7] overenergetic replacement therapy,[8] and diabetes insipidus,[9] there is no doubt that lesions of the central nervous system account for most of the recorded cases.[3 10–13] W. W. Engstrom and A. Liebman[9] studied the response to pitressin of a woman with diabetes insipidus and hypernatraemia. They found that she responded well to pitressin by retaining large amounts of water, but that on withdrawal of the hormone water diuresis promptly appeared and the hypernatraemia recurred. Her water intake did not vary before, during, or after treatment with pitressin. They concluded from this that the normal thirst mechanism was impaired, and suggest that many of the recorded cases of hypernatraemia complicating cerebral lesions may be due to unrecognized diabetes insipidus with or without impairment of normal thirst mechanism. Unfortunately many of the recorded cases were not only incontinent of urine, so that exact

[1] Schoolman, H. M., *et al.*, *Arch. intern. Med.*, 1955, **95**, 15.
[2] Borst, J. G. G., *Acta med. scand.*, 1938, **97**, 68.
[3] Allott, E. N., *Lancet*, 1939, **1**, 1035.
[4] Nadal, J. W., *et al.*, *J. clin. Invest.*, 1941, **20**, 691.
[5] Marriott, H. L., *British Medical Journal*, 1947, **1**, 285.
[6] Luetscher, J. A., and Blackman, S. S., *Ann. intern. Med.*, 1943, **18**, 741.
[7] Goodale, W. T., and Kinney, T. D., ibid., 1949, **31**, 1118.
[8] Merivale, W. H. H., *Proc. roy. Soc. Med.*, 1954, **47**, 992.
[9] Engstrom, W. W., and Liebman, A., *Amer. J. Med.*, 1953, **15**, 180.
[10] MacCarty, C. S., and Cooper, I. S., *Proc. Mayo Clin.*, 1951, **26**, 185.
[11] Cooper, I. S., and MacCarty, C. S., ibid., 1951, **26**, 354.
[12] Higgins, G., *et al.*, *Lancet*, 1951, **1**, 1295.
[13] Peters, J. P., *New Engl. J. Med.*, 1948, **239**, 353.
[14] Lewy, F. H., and Gassmann, F. K., *Amer. J. Physiol.*, 1935, **112**, 504.
[15] Kary, C., *Virchows Arch. path. Anat.*, 1924, **252**, 734.
[16] Sweet, W. H., *et al.*, *Res. Publ. Ass. nerv. ment. Dis.*, 1948, **27**, 795.
[17] McLardy, T., *J. Neurol. Neurosurg. Psychiat.*, 1950, **13**, 106.
[18] Livingston, R. B., *et al.*, *Res. Publ. Ass. nerv. ment. Dis.*, 1948, **27**, 405.

figures for urinary output could not be given, but also unconscious, so that it was impossible to tell whether they were thirsty or not.

It has been found in animal experiments that hyperchloraemia and very low excretion of renal chloride can be produced by lesions of the paroptic nucleus of the hypothalamus,[14] and this nucleus has been shown to be related functionally to the pars nervosa of the pituitary.[15] In man operative interference with the frontal lobes of the brain has been followed by hypernatraemia and hyperchloraemia.[16 17] Although all the patients described by G. Higgins *et al.*[12] had damage to their frontal lobes, they also had extensive lacerations in other parts of the brain, especially the temporal region. J. H. Cort (in R. B. Livingston *et al.*[18]) has produced the renal shunt of Trueta in cats by stimulating the posterior hypothalamus, the sensorimotor cortex, and area 13 on the orbital surface of the frontal lobes. These experiments and the clinical evidence suggest that hypernatraemia is a rare and interesting complication of a wide variety of cerebral dysfunctions, not necessarily confined to one area of the brain.

TOBACCO AND THE BALLISTOCARDIOGRAM

The ballistograph is an instrument which records body movement occurring with each heart beat, and the tracings of the ballistic waves can be used to provide information about cardiac output. High-frequency ballistocardiography has demonstrated striking though temporary circulatory changes following smoking, and, while these pathological reactions to nicotine occur in a number of healthy persons, over half the patients with coronary disease tested in this way show definite deterioration in the pattern of the tracing. Russek and his colleagues[1] confirm these observations of Henderson[2] and Davis,[3] but attribute the results to peripheral vasoconstriction rather than to coronary arterial spasm. Unlike the electrocardiogram, the ballistocardiogram is not modified by cardiac abnormalities alone but to an equal or greater extent by vascular changes. Trinitrin was as ineffective in preventing ballistic deterioration from tobacco as Graybiel[4] had found it to be in reversing electrocardiographic T-wave depression produced by the same agency. Whisky, on the other hand, abolished or masked abnormal responses to smoking, and from what is already known of the principal point of action of both drugs it is clear that the antagonism between alcohol and nicotine takes place at the periphery, especially in the skin vessels.

In attempting to find an answer to the question why the majority of patients with coronary disease show similar ballistographic changes to those of normal subjects who are known to be hypersensitive to tobacco, Russek suggests that overt or latent cardiac insufficiency in these cases is brought to light by minor degrees of peripheral vasoconstriction. Buff,[5] working with apparently normal subjects only, reaches a similar conclusion. He found that hypersensitivity to one cigarette, as shown by the ballistocardiograph, occurred in 15% of those between 30 and 40 years of age as against 5% in those under 30. He attributes the difference to latent coronary disease in the older group and intends to continue the study of those who showed an abnormal response, whom he has strongly advised to give up smoking forthwith.

Screening tests of this nature are largely empiric, since they impose a circulatory burden with a wide idiosyncratic variation on a heart which may or may not be affected directly by the drug. They cannot be applied to more than small numbers of normal smokers or patients with coronary disease. They have, however, given clear instrumental support to the entity of "tobacco heart" and serve again to remind physicians of the possibility of this diagnosis in disorders of cardiac function. Earlier this year we commented on statistical investigations into the association between smoking and coronary thrombosis.[6] The finding of increased susceptibility to the effects of smoking among patients with the disease will strengthen the opinion that the vascular and respiratory effects of the habit impose an additional load on the heart, and that the patient should be made aware of this.

[1] *J. Amer. med. Ass.*, 1955, **157**, 563.
[2] *Brit. Heart J.*, 1953, **15**, 278.
[3] *Amer. Heart J.*, 1953, **46**, 529.
[4] Ibid., 1938, **15**, 89.
[5] *J. Amer. med. Ass.*, 1955, **157**, 569.
[6] *British Medical Journal*, 1955, **1**, 91.

EDITOR, "CANADIAN MEDICAL ASSOCIATION JOURNAL"

At the Annual General Meeting of the Canadian Medical Association on June 22, Dr. Norman H. Gosse, Chairman of the Council of the C.M.A., paid a most felicitous tribute[1] to Dr. Hugh Ernest MacDermot, the retiring editor of the *Canadian Medical Association Journal*. Dr. MacDermot, who graduated at McGill University, and was at one time on the staff of Montreal General Hospital, began his connexion with the *C.M.A. Journal* in 1923, when Dr. A. D. Blackader was editor, and he later became assistant to Dr. A. G. Nicholls, whom he succeeded as editor in 1942. Under his wise and skilful guidance the *C.M.A. Journal* has gone on from strength to strength and has reached the point at which this success has justified changing the frequency of publication from once to twice a month. Dr. MacDermot has maintained the highest standards of medical journalism in Canada, and by this example has fostered the high standards of the individual Canadian doctor. The *C.M.A. Journal* has become increasingly familiar to English readers, and those who know it and its now retiring editor will echo this part of Dr. Gosse's citation: "He has done much for the journal; and we are happy to pay him this tribute: that it was under his editorial leadership and, as we believe, because of his fine sense of the fitness of things that the journal has won the high esteem and respect that it now enjoys, not only in our own land, but possibly even more so in those other lands in which it is known."

In extending wishes for a happy retirement to Dr. MacDermot, we acclaim as his successor Dr. S. S. B. Gilder, formerly on the staff of *Abstracts of World Medicine*.

[1] See *Supplement*, p. 11.

EMERGENCIES IN GENERAL PRACTICE
ACUTE ANXIETY AND HYSTERIA

BY

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Anxiety is an abnormal emotion which resembles fear subjectively but differs from it in its persistence when the cause of the emotion is no longer apparent to the patient or appears inadequate to account for the symptoms experienced. It is abnormal by the criteria we apply to illness generally—namely, that the patient is called to bear an unreasonable amount of discomfort and is disabled to a varying degree in his work and in his capacity to maintain satisfactory social relationships. Thus the definition of the term excludes the normal or physiological response to the buffets of everyday life, and in practice there is no difficulty in distinguishing the two. A distinction must also be made between anxiety the symptom, which may colour a number of syndromes, and the anxiety state, which is a fairly clearly demarcated syndrome with anxiety as its principal symptom.

When anxiety is very severe it overflows into the muscular system, with the production of gross motor restlessness, and it is then termed "agitation." Agitation is always a symptom of an illness of a serious kind, and most patients referred urgently with a diagnosis of "acute anxiety state" are in fact suffering from a depression. Self-reproach and hopelessness about the future will usually be in evidence, and a depressive illness should always be suspected when symptoms of anxiety develop within a period of weeks without obvious external cause, and particularly when the patient is middle-aged or elderly. In younger patients acute anxiety or agitation may be the presenting symptom in schizophrenia, and the specific symptoms of that condition must be looked for. There may be paranoid ideas, woolliness or bizarreness of thought, or auditory hallucinations; and relatives may give a history of behaviour which has been unmistakably psychotic.

Symptoms of Anxiety

Whether anxiety develops as a primary symptom or as a reaction to another psychiatric illness altogether, it will produce bodily symptoms of a troublesome kind. Tension will develop in the voluntary musculature, notably in the front or back of the head and in the neck. Pain may come and go or the patient may find that because of one kind of discomfort or another his head is in his consciousness all day long. When muscle tension is severe and diffuse there is some reason to suppose that the massive central bombardment by proprioceptive impulses is responsible for the phobic attacks which afflict some patients from time to time. These are feelings of intense anxiety amounting to panic, and they are particularly likely to occur when free motor expression is denied by circumstances, as when travelling in a train or sitting in church. The attacks can be dispelled by deliberate relaxation of the musculature, but this will only be possible in a patient who has been taught how to go about it.

Other symptoms will result from the action of an excitable autonomic nervous system upon the viscera. It is wrong to look upon the symptoms of anxiety as being due predominantly to an overactive sympathetic, for in fact both divisions are working excessively and in a state of uncertain and fluctuating equilibrium. Thus the pulse will be labile but will not show a sustained change of rate. Constipation and diarrhoea may alternate with one another and the colour of the skin may alternate from pallor to flushing. It is the uncertain and variable behaviour of his organs which alarms the patient more than anything else and focuses his attention on one part, with the production of symptoms such as palpitations or epigastric discomfort.

Treatment

With two exceptions, a simple anxiety state will rarely call for emergency treatment. Occasionally a headache may prove intractable and severe enough for the doctor to be sent for, and headaches of this kind differ from "migraine" only in the absence of visual phenomena which have long been regarded as non-essential to the diagnosis. The treatment consists of a sedative such as sodium amylobarbitone in a dose of 3 gr. (0.2 g.), together with aspirin, 10 gr. (0.65 g.). There is no advantage in giving aspirin in larger doses than this, though of course it may be helpful to repeat the dose in an hour. The patient should lie down; when feasible, quiet and darkness will help in reducing the sensorial bombardment. The second condition for which the doctor's help may be sought is the panic attack, particularly when it occurs at night. What happens is that a very tense patient lies down and tries to keep still enough to go to sleep, and the denial of motor outlets provokes the attack. The immediate need in an anxiety attack is for a powerful and quickly acting hypnotic, and again sodium amylobarbitone is one of the more suitable, in doses of 3 to 6 gr. (0.2 to 0.4 g.) according to the severity of the attack and the weight of the patient.

When acute anxiety or agitation is combined with depression which is not itself slight or transient we are dealing with a dangerous combination. The depression makes life insupportable and the anxiety makes a solution an immediate necessity. The only possible solution to his problems may seem to be death, and the risk of suicide is great. It is at its height in the early morning, when symptoms are at their worst. If the patient's life appears to be in danger he should be placed under supervision, if necessary against his will, as quickly as possible. In the case of an ordinary patient the help of the duly authorized officer should be sought. He is a lay officer of the local health authority who has to decide for himself that the patient is mentally ill, and that by reason of this should be placed under restraint. Since the decision and the responsibility are the D.A.O.'s, the doctor should not be put out if the officer does not always follow his advice. In practice these officers discharge their duties with tact and helpfulness, and will not usually differ from a doctor who has taken reasonable care in his examination.

The patient will either be sent to an observation ward in a general hospital which has been recognized for the purpose, on what is called a "three-day order," or he will be sent straight to a mental hospital on an urgency order. In the case of a patient who is to be sent to a private hospital or licensed house the urgency order is used, but in this case the nearest relative will sign it and the services of the D.A.O. are not required. Any doctor may provide the medical certificate which goes with the order, though in practice it is usually filled in by a psychiatrist called out to see the case. The order forms may be obtained from any law stationer, and are self-explanatory. A diagnosis should not be included in the certificate, and non-technical language should be used. The doctor is well protected from vexatious litigation provided he acts in good faith and

exercises reasonable care. If the D.A.O. is expected it is sometimes unwise to give sedatives that may cover up the psychotic features which it is desired that he should see. The relatives should be warned in clear terms of the suicidal risk and the onus placed upon them of ensuring the patient's safety when that is a reasonable course to adopt. If sedation is imperative 6–9 gr. (0.4–0.6 g.) of sodium amylobarbitone can be given by mouth, or if the patient will not swallow, 5–10 ml. of paraldehyde intramuscularly is both safe and effective. Ampoules of 5 ml. of paraldehyde can be purchased in boxes of six, and do not deteriorate when carried in a bag over quite long periods.

Hysteria

Hysteria is a condition in which mental or physical symptoms not of organic origin are produced and maintained by motives which in some part, at least, are unconscious ones. If the motives involved are fully conscious we are, of course, then dealing with malingering. It has been customary to add to this definition the element of "real or fancied gain" which is to be derived from the symptoms. This gain is not always easily discerned, and certainly it may not be financial or material at all except in a very subordinate way. Thus in anorexia nervosa, which is more commonly hysterical than not, there is frequently no motive which makes any sense apart from a settled determination upon self-destruction, in which the patient is sometimes successful. The same applies to the strange hysterical self-mutilations which are sometimes encountered.

There are three notable features common to most hysterical reactions. First, there is the remarkable dissociation of mental and bodily functions from the main stream of living, which permits a patient weighing less than 5 stones (32 kg.) to sit cheerfully in bed quite unconcerned about the failure of her treatment, while another mentions casually that he "went blind yesterday and just hasn't seen a thing since." Such dissociation explains or perhaps merely reformulates the remarkable analgesias seen in some hysterical patients, and which are sometimes readily produced in hysterical personalities by hypnotists whether on the stage or in the consulting-room. The second characteristic lies in the suppressed emotion in hysterics, which may be liberated in a disconcerting way as a result of therapy which is a little too vigorous in its early stages. The third feature is a derivative of the second, and has been referred to as a tendency to "short circuit." A sudden liberation of pent-up emotion in the absence of cortical control may produce hysterical outbursts, hysterical delirium, or a hysterical fugue.

Hysteria should always be treated with caution until the reaction has been fully assessed and the diagnosis is secure. Apart from the problems set by a short-circuit, a hysterical reaction may conceal quite serious affective disorder. Involutional depressions quite often present with what look like hysterical syndromes, and a failure to recognize the underlying and more important condition may be serious. Hysterical reactions are liberated by organic disease much more often than is serious affective disorder, and while the diagnosis of hysteria may and should be made on its own symptoms and signs, a careful physical examination is required to exclude precipitation by organic diseases. Thus hysterical reactions often develop on top of disseminated sclerosis or complicate the disability left by a cerebral vascular accident.

Acute Somatic Hysteria

Paralysis of a limb or of one side of the body will not usually require emergency treatment, though the doctor may be pressed by the patient or relatives to see the case immediately. The patient will show positive signs of his disease, and in particular that remarkable unconcern which is known as *belle indifférence*. There may be a history of previous attacks and the precipitants of the present one may become evident when inquiry is made. There may be signs and symptoms of underlying anxiety—a history of sleeplessness, or a fine tremor of the hands. Physical disease of the nervous system is eliminated by showing its intactness even though equality of the deep reflexes is the most that can be shown in an uncooperative patient. Hysterical blindness shows the triad of a sudden onset, normal fundi, and normal pupillary reactions. Hysterical aphonia soon gives way to whispering, which is more convenient for the patient, and it may be observed to be selective and pitched so that it causes maximum irritation while permitting social or therapeutic exchanges.

If they are of recent onset, these conditions can usually be cleared up quickly with the aid of intravenous sodium amylobarbitone or thiopentone, which permits the discharge of suppressed emotion and the reception of suggestion while in a state of clouding. Equally good results may be obtained by some without the help of drugs at all, and this is preferable in general practice. A confidence born of having dealt successfully with similar cases before, mixed with an unprovocative aplomb, are the essential ingredients of such an approach. If this fails or for any reason is not tried, then it will suffice to treat the condition conservatively until psychiatric advice can be obtained.

Hysterical fits are sometimes confused with epilepsy though they differ in almost every particular. A hysterical fit does not show the characteristic tonic and clonic phase of epilepsy, and movements are haphazard or sometimes quasi-purposive. The tongue is not bitten, injury is seldom inflicted on the body, and incontinence is rare. The fits are circumscribed in time, and the short-term treatment lies in sedation pending investigation of the condition.

Hysterical Fugues

Fugues refer to wandering states for which the patient subsequently claims an amnesia. When the attack is unassociated with affective disorder such as depression, it is usually in the nature of a short-circuit reaction. Following some domestic upset perhaps, the patient will have a violent emotional scene and leave his house. It is virtually certain that such states of dissociation last only for a very short time, and that the main part of the fugue is not really so at all. A man arriving home three days late from his work may find loss of memory a good deal simpler as an explanation than the true one, both to his wife and to his employer. It is not always helpful to his affairs to be obsessionally preoccupied with the establishment of the truth, and it may be wise to be content with conveying silently, and with civility, one's conviction that he is a liar. The wanderings of depressives, which are sometimes regarded as hysterical, are in quite a different category. A depressed patient may wander for days in a state of preoccupation bordering on stupor and may have an amnesia subsequently which is to be ascribed to failure to register events. His behaviour during the journey will, on inquiry, lack the integration present in the hysteric. He will have had little or no food, and will show neglect of his person and clothing. Sometimes a friendly policeman will find him, and inquire whether he has lost his memory; this may suggest a reasonable explanation to the patient of what has happened. Some of these wanderings by depressives are begun with the intention of committing suicide when the necessary courage has been summoned or the necessary despair accumulated.

In the case of the hysteric, treatment can be undertaken with intravenous drugs, but in fact the amnesia can be unravelled in most cases without them. A firm conviction that the condition does not happen can be transmitted to the patient without much difficulty, and the problem is then resolved into the treatment of the underlying affective state if it is severe enough to require it.

Hysterical Stupor

Stupor is found, when it is found at all, in chronic and practised hysterics, and it can cause anxiety from the diagnostic point of view to the most experienced observer. The patient may lie flaccid and as if in coma, with a total absence of psychologically understandable responses to

stimuli as the usual definition of coma requires. It is called stupor rather than coma, because there is good evidence—usually retrospective—that awareness has not been suspended. Nevertheless the dissociation of function is so well established that there may be no response to pinches, sharp needles, or any other stimulus which it would be acceptable to apply. There is one common but not invariable sign which should be looked for since it gives the diagnosis, and that is a slight rapid fluttering of the eyelids. Most organic causes of coma can be excluded by an ordinary physical examination which may have to include catheterization and examination of the urine. The history of the last few hours will suffice to eliminate narcotic poisoning, epilepsy, and head injury, save in those few cases where no history at all is available. Fortunately in most hysterics there will be available a history of previous dissociative episodes, which will vary from the vague to a clearcut statement that the patient is just "having another of her trances."

A patient in a hysterical stupor is best left alone provided the diagnosis is clear, for the condition will usually resolve in a few hours or overnight. If there is any suspicion that barbiturates have been taken as a gesture additional to the stupor, then no risks should be taken and the stomach should be washed out, unless the dose taken is known with certainty to be innocuous.

Next article on Emergencies in General Practice.—"Treatment of Severe Haemoptysis," by Dr. F. H. Young.

Refresher Course Book.—Copies of the second volume of collected articles from the Refresher Course for General Practitioners are still available at 25s. (postage 1s.) each. The first volume is now sold out.

Clinical Pathology Book.—"Clinical Pathology in General Practice," a collection of 39 articles on clinical pathology that appeared in the *Journal* as part of the Refresher Course for General Practitioners, is now available, price 21s. (postage 9d.).

Both these volumes are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

THIRD EUROPEAN RHEUMATOLOGY CONGRESS

[FROM A SPECIAL CORRESPONDENT]

The third European Rheumatology Congress was held from June 13 to 17 at Scheveningen, in Holland, under the presidency of Dr. PEDRO BARCELO (Spain). Eight hundred delegates of the European League against Rheumatism attended, among whom were a number of rheumatologists from this country.

One of the main themes was the association of rheumatism and social medicine. Professor K. M. WALTHARD (Geneva), among others, described the services and plans for the future in Switzerland. A small survey had been carried out in one of the most rural Swiss valleys, where it was found that degenerative arthritis was extremely common. This was ascribed to the hard manual labour undertaken by the inhabitants.

Prognosis in Rheumatoid Arthritis

Professor NANA SWARTZ (Stockholm) presided over a session devoted to the evaluation of therapy, at which Dr. J. J. R. DUTHIE (Edinburgh) described the significant factors in reaching a prognosis in rheumatoid arthritis. He based his opinion on a follow-up study of 282 patients seen at an average of four years after discharge from hospital. Patients admitted to hospital within one year of onset had a much better prognosis than those admitted at a later stage. Functional capacity at follow-up deteriorated progressively the longer the duration of the disease before admission, and those patients in whom the disease ran a rapidly progressive course in the first year fared appreciably better in the long run than those in whom it started more insidiously. The importance of studies on the natural history of rheumatoid arthritis, particularly now that the necessity for evaluating new drugs has arisen, was admirably stressed in this paper.

During a session on connective tissue, with Professor F. COSTE (Paris) in the chair, Dr. L. E. GLYNN (Taplow) described studies suggesting that there is a widespread alteration in connective tissue in patients with rheumatic fever. There was increased permeability of their connective tissue, as shown by the delay in the reconstitution of the dermal barrier following an injection of hyaluronidase. Dr. G. ASBØE-HANSEN (Copenhagen) discussed the hormonal control of mesenchymal tissue. He had found that the individual elements of all connective tissue respond alike to the same hormones. In the course of a few hours endocrine secretions could alter the physicochemical balance and water-binding capacity of the tissues, and accumulation of mucopolysaccharides reduced tissue permeability. Thyroid hormone inhibited wound healing. The adrenal cortical hormones regulated the function of the mast cells: these cells, believed to be the source of ground-substance components, underwent changes such as degranulation and vacuolation, and their sulphur turnover was altered, while the release of hyaluronic acid, heparins, and histamine might also be affected; corticotrophin had the same effect. In patients with rheumatoid arthritis the mast cell count in the synovial tissue was increased, but this rise was inhibited by cortisone and corticotrophin.

Dr. W. S. C. COPEMAN (London) presided over a session devoted to papers on disk degeneration and osteoarthritis of the spine. Professor STEN FRIBERG (Stockholm) showed that the lower lumbar disks disintegrate earlier and to a greater extent that has previously been supposed, nor did a negative radiograph preclude even advanced disintegration. Deforming arthritis in the intervertebral joints occurred mainly at the level of the disk trouble which was found in 50% of patients with chronic lumbar pain. In a large series of such patients 20% reported an injury accepted for insurance compensation, 20% gave a history of minor strains such as lifting, and 60% had no obvious exciting cause.

The delegates were entertained by the Government of the Netherlands in the Hall of Knights at The Hague, and by the Corporation of Amsterdam at the Rijksmuseum following a trip on the canals.

The number of war pensioners fell by 30,882 to 900,141 during 1954, states the *Report on War Pensioners* published on June 28 (H.M.S.O., price 4s.). This is the first annual report under the arrangement by which the pensions are administered by the Ministry of Pensions and National Insurance, and the medical and surgical treatment by the Health Departments. At the end of 1954, 367,000 were receiving disablement pensions for the 1939 war, 273,335 for the 1914 war, and 38,700 for post-war service. 75,593 widows from the 1939 war received pensions, 91,986 from the 1914 war, and 86,364 received grants for their children. For the financial year ending March 31, 1954, £82,460,891 was spent on war pensions and allowances, and the increased rates which came into effect in February this year will raise the total cost by £15m. A second and final payment of £28 was made to British Far Eastern prisoners of war and civilian internees from the realization of Japanese assets in the U.K., and a share of the proceeds from the sale of the Burma–Siam railway was distributed among Servicemen prisoners. Medical boards examined 118,650 pensioners, but of the 1939 group 70% did not have their assessment altered. Full employment meant a drop in the use made of welfare services.

British Medical Association, Canadian Medical Association, and Ontario Medical Association

JOINT ANNUAL MEETING, TORONTO, 1955

SUMMARY OF PROCEEDINGS

SECOND GENERAL SESSION

Simplicity in Anaesthesia

The newly elected President of the B.M.A., Dr. T. C. ROUTLEY, occupied the chair for the second general session, on June 23, when Professor Sir ROBERT MACINTOSH (Oxford) made "A Plea for Simplicity in Anaesthesia." He believed that in many circumstances anaesthetic apparatus was unnecessarily complex, especially outside the larger medical centres. It was true that the field of surgery and the safety of the patient might be jeopardized by the absence of a few pieces of anaesthetic equipment, but he doubted whether the development of apparatus along "battleship" lines indicated progress. Nitrous oxide and cyclopropane were useful, but not indispensable. He would therefore describe simple, light equipment which did not rely on cylinders. The modern approach was to give light general anaesthesia to ensure unconsciousness and then to abolish reflex response to stimuli by a relaxant. Here Sir Robert paid a tribute to Dr. H. R. Griffith, of Montreal, for the introduction of curare into anaesthesia. The relaxants, he continued, were safe in competent hands, provided that a vein was kept open for intermittent injections. This was most conveniently done by having a Mitchell needle strapped into a vein on the dorsum of one hand.

If he had to give priority to any one piece of apparatus, said Sir Robert, it would be the small bellows, with unidirectional valves in the supporting base, for assisting or controlling respiration. The use of the bellows for artificial respiration meant that an oxygen cylinder was not a necessity when the respiratory muscles were paralysed. In fact, air was safer than oxygen in such circumstances, because the latter might mask deficient pulmonary exchange. If an inhalation agent were desired in addition, gas and oxygen could be run in through the tap at the base of the bellows, or the inlet could be covered with gauze on which any liquid anaesthetic could be dropped. Alternatively, a vaporizer could be attached for ether or "trilene." For most operations air was excellent for oxygenating the patient, but for intrathoracic surgery the lungs were seldom fully inflated, since this interfered with access to the field. In such operations supplementary oxygen was essential to compensate for the decreased aeration.

Sir Robert concluded by correcting two common misconceptions. First, controlled respiration by positive pressure could be satisfactorily carried out without an endotracheal tube. And, secondly, closed-circuit anaesthesia was not essential to the maintenance of controlled respiration; this had been amply shown on victims of poliomyelitis.

Caesarean Section

Professor DUGALD BAIRD (Aberdeen) discussed "Caesarean Section; Its Use in Difficult Labour in Primigravidae." He said that after the onset of labour the risks of section increased steadily with the duration of the labour, particularly after 48 hours. The mortality in such cases was higher in primigravidae, in whom the prolongation of labour was usually due to anomalies of uterine action. The modern tendency to avoid difficult vaginal delivery in prolonged labour by the freer resort to section was safer for the child and probably also for the mother. Professor Baird illustrated this point by statistics from all first births in the city of Aberdeen from 1939 to 1954. The stillbirth rate from birth trauma and from unexplained causes in mature babies fell steadily during this period, partly because of increased hospitalization and partly because of the more frequent resort to caesarean section, especially in the older primigravidae. The section rate for primigravidae rose from 1.1% in 1938–42 to 3.8% in 1951–4. The incidence of difficult labour increased with age, as did the tendency to unexplained intrauterine death of the mature foetus, so that the baby of the elderly primigravida was doubly jeopardized. In Aberdeen they had therefore employed section more freely in primigravidae, so that in 1948–54 the rate was over 27% in the over-35 age group and over 9% in the 30–34 age group. This had resulted in a marked fall in stillbirths from birth trauma and from unexplained causes. The chief indication for section had been difficult labour; but postmaturity, foetal distress, maternal age, and low fertility were other important indications. It was of interest that a small-scale inquiry had shown that in all age groups the performance of a section in the first labour decreased the likelihood of a second pregnancy; but a first forceps delivery did not have the same deterrent effect.

Professor Baird concluded that placental and uterine function became steadily less efficient from the age of 25, especially if postmaturity were an added complication. What was wanted was the lowest stillbirth rate and the lowest section rate. In his experience the optimum section rate in primigravidae was between 3 and 5%, but it must vary with the age composition of the patients and the health and nutrition of the community.

The General Practitioner and the Laboratory

Dr. WILLIAM PICKLES (Aysgarth, Yorkshire) discussed "The General Practitioner and the Laboratory." He said that early in his career as a general practitioner he had decided to interest himself in epidemic disease, particularly in incubation periods, duration of infectivity, and mode of spread. Some conclusions could be reached solely on clinical grounds, but for a more complete picture the help of a pathologist was required. In 1929 during a large epidemic of infectious jaundice he had used the good services of the public health laboratories and the Wellcome Research Institution. He was thus able to disprove a theory, then current, that these cases were mild forms of Weil's disease, for in the latter there was a polymorphonuclear leucocytosis, while his cases showed a relative lymphocytosis. More recently it had been shown that the infective agent of epidemic jaundice could be recovered from the stools of patients, the nasal insufflation of a dried preparation of which could infect fresh volunteers. But he himself had previously concluded that droplet infection was the common mode of spread, and he still held this view.

In 1932, continued Dr. Pickles, he had encountered a pandemic of diarrhoea and vomiting. With laboratory help the causative organism was shown to be that of Sonne dysentery. In 1947 he had seen what he still maintained, and with good support, was an epidemic of a form of glandular fever. A transient rash occurred, followed by general glandular enlargement, but in no case was the Paul–Bunnell reaction positive. Other conditions he had investigated were "farmer's lung"—a relatively benign mycosis—and Bornholm disease. Dr. Pickles then cited three deaths, all of which could easily have been ascribed to coronary thrombosis, but which the pathologist had shown to be due to acute lobar pneumonia, rupture of a dissecting aortic aneurysm, and acute pancreatitis respectively. The help obtainable now from the local laboratory, he concluded, not only benefited the individual patient but enabled the practitioner to obtain a more comprehensive picture of diseases.

PANEL ON THE NATIONAL HEALTH SERVICE

Wednesday, June 22

Despite the competition of many Section meetings, interest in the British National Health Service drew a large audience to hear contributions from four speakers on different aspects of that service. Dr. R. W. RICHARDSON (Winnipeg) took the chair.

Historical Background

Dr. E. A. GREGG (London) began by giving the historical background of the development of general practice in Britain during the past 40 years. Beginning with the picture of urban practice before the days of national health insurance, he went on to speak of the evolution of general practice under national health insurance arrangements, stressing the British Medical Association's own contributions to the planning of the developing health service. He mentioned the work of the Medical Planning Commission of the B.M.A. and how this work was already far advanced before the publication of the Beveridge report, which in its turn led to the Parliamentary preparation of a Bill for a comprehensive health service for the nation. He told his audience about the negotiations that took place at this time between the profession and the Government; about the plebiscites of the profession, which showed marked opposition to the scheme in its original form; about the prolonged discussions, with the Minister at first obdurate, but later willing to accept important modifications in the scheme. He spoke of the principles which the profession enunciated as being necessary to doctor and to patient alike for the satisfactory working of the new service, and said that it was only when the profession was satisfied that the agreed modifications safeguarded these principles that it accepted the service that started in 1948.

General Medical Services

Dr. A. TALBOT ROGERS (Bromley) spoke next. He emphasized that one of the chief aims of the doctors who negotiated for the profession was to ensure that the service should be of a kind which preserved the maximum clinical and administrative independence for the doctors. Speaking for the general practitioners, he felt that he could say, after seven years' experience of the new service, that they had achieved a remarkable degree of clinical and administrative freedom. He believed that the reason for this lay in the wide administrative responsibilities which the practitioners themselves had willingly accepted.

Dr. Rogers went on to explain to his Canadian audience the administration of the general-practitioner service through executive councils, and stressed the greatly increased amount of work and responsibility now falling on the local medical committees. He described how the B.M.A.'s General Medical Services Committee, fortified by the authority of the Council of the Association and the Conference of Local Medical Committees, exercised central executive power in direct negotiation with the Government on all day-to-day matters concerning the general practitioner working inside the service. He gave several examples of negotiations successfully carried out with the Government on such matters as remuneration, prescribing, and the hearing of complaints against doctors. He also mentioned that the G.M.S. Committee had persuaded the Government that the inspection of the doctors' surgeries, which it had originally been suggested should be entrusted to executive councils, could be carried out more properly and more effectively by the doctors' own colleagues.

Methods of liaison between the different sections of the profession were developing, Dr. Rogers said, in a way that would allow it to walk in step and to present to the Government of the day views which could be endorsed and accepted by all.

Hospitals and Consultants

Dr. T. ROWLAND HILL should have been the third speaker, but illness had unfortunately prevented him from travelling to Canada. His paper was read by Mr. NICHOLSON LAILEY (Taunton). Dr. Hill referred to the history of British hospital and consultant services, mentioning the fine tradition of service in the voluntary hospitals and the gradual supplementation of this voluntary work by municipal hospitals. He stressed the virtual separation of these two types of hospitals until 1939, when the Emergency Medical Service successfully provided for their collaboration under wartime conditions. Dr. Hill commended the unification of the hospital system under the National Health Service, but, while giving praise to this unification, he warned that it was important to ensure that there should not be any loss of the opportunities that the voluntary hospitals had afforded for participation by the medical staff in the planning and administration of their own hospitals. The degree of opportunity which different groups of hospital consultants now had for such work varied considerably in different parts of the country, and in many places left much to be desired.

Proper junior staffing of hospitals, particularly in hospitals distant from the university centres, was a problem. There had undoubtedly been some loss of association between the practitioners and the hospitals as a result of the coming into being of the new service, and ways might have to be found for more use of properly trained general practitioners in hospital work.

Dr. Hill reported that the total cost of the National Health Service amounted to one-tenth of the national income, and of this large sum nearly three-quarters was needed to pay for the hospital service. With a fixed financial budget and increasing costs for wages, for food, fuel, etc., there had been considerable difficulties in maintaining the hospital service. There had been very little spare money for capital extension or new hospital building. Now the outlook seemed a little better and many much-needed developments were being put in hand. Consultants, however, felt that it was not only new buildings that were needed but also that there were still fewer consultants than there should be if the best service was to be given to the country.

With an ageing population, they could not feel content with the facilities available for the chronically disabled sick or those disabled by old age. Dr. Hill felt that insufficient money was available for the encouragement and development of medical research, and that money spent on this, and on maintaining high standards of practice and teaching in the hospitals, would ensure better services for the future. Dr. Hill ended by saying: "The medical men and women who staff our hospitals are not in any way downcast, but are finding the present conditions definitely stimulating, and a note of optimism and of confident progress is to be heard more loudly than in many years in Great Britain."

Public Health

The fourth contribution, dealing with the public health services under the National Health Service, came from Dr. S. C. GAWNE (Liverpool). He began by mentioning the tripartite administration of the health service and went on to tell his audience of the many functions carried out by the local health authority, particularly in the preventive services and in the field of health education and the teaching of mothercraft. He spoke of the domiciliary maternity services and the co-operation that was being achieved between the local authority services and the general practitioners in this field. There had been a steady increase in hospital confinements during recent years, this being due more to economic than to medical reasons. He again emphasized the importance of co-operation between the general practitioner and the preventive services when he spoke of the ancillary workers in the fields of home nursing and health visiting.

Dr. Gawne had hoped to see the development of health centres, where the work of the general practitioner, the consultant (in his domiciliary visits), and the preventive services might have found a focal meeting-place. Unfortunately, little progress had yet been possible in this field, although a few centres of an experimental type had been built and were operating. It seemed likely that the development of

group practice, carried out from the doctors' own premises, was much more likely to be the pattern of future practice than the health centre concept, which had seemed at one time likely to take a foremost part in British medical practice. He hoped that it would be possible to encourage co-operation between the local health authority services and these group practices. He too spoke of the problem of the ageing population, and said that the general policy of the medical officers of health was to encourage old people to stay as long as possible within the familiar surroundings of their own homes rather than to transfer them to special homes under the care of the local health authority. Every assistance that could be given to them by the local authority in the way of nursing, home help, night help, and health visiting that would help them to remain self-sufficient was very well worth while.

Questions Answered

Following the papers many questions were asked by the audience and answered by the speakers. They ranged from inquiries about the amount of paper work the doctors had to do, the number of people they had to see at each surgery, and the opportunities available for general practitioners to work in hospitals, to the ease or difficulty which young doctors found in entering general or specialist practice, the effects of deficiencies of finance upon the clinical efficiency of hospitals and the possibilities of exchange of practices, particularly with regard to the possibility of a man working in his earlier life in an industrial area and later moving to a less exacting type of practice.

Such a list of questions—and there were many others—showed that Canadian colleagues had taken a keen and intelligent interest in the progress of our Service.

THE SECTIONS

SECTION OF MEDICINE

Wednesday, June 22

Simple Obesity

Under the presidency of Dr. W. DE M. SCRIVER (Montreal) Dr. E. R. CULLINAN (London) discussed the essential nature, the effects, and the treatment of simple obesity. He said that there was no adequate definition of obesity, and the average weight-for-age tables of the life insurance companies were not altogether satisfactory. The Metropolitan Life Insurance Company had therefore prepared tables with no distinction for age after 25 years, giving a range of desirable weights for three groups of differing build—slight, medium, and heavy.

Simple obesity was always caused by an excess of calorie intake over output, but there remained a constitutional problem in which inheritance might play a part—for example, the type of maternal obesity described by Sheldon was constitutionally determined. No abnormal metabolic pathway such as occurred in Cushing's syndrome had yet been described in the obese. Appetite was controlled by the hypothalamus, and R. A. McCance had shown that this control was very exact, most adults getting it right to about 1 g. daily. Psyche influenced these hypothalamic centres, but the chemical mechanisms underlying appetite and hunger were not yet defined. Although Kekwick had shown that a low-calorie diet with a relatively high fat content was effective in weight reduction, diets of carbohydrate restriction were more practicable. There was no doubt that excessive weight produced morbidity and increased mortality rates, and physicians did their obese patients a disservice if they did not persuade them to eat less. Dr. Cullinan reviewed dietary schemes (including those of Mr. William Banting in 1862) and stressed the need for increased exercise, which did not have to be violent but must be undertaken daily. Amphetamine was the only drug which had value in the treatment of obesity.

Idiopathic Steatorrhoea

Idiopathic steatorrhoea was discussed by Professor A. C. FRAZER (Birmingham) and defined as the passage of fatty, fluid, offensive, frothy stools. The average normal stool contained less than 5 g. of fat; to make a diagnosis of steatorrhoea a daily diet containing 50 g. of fat should be used. In steatorrhoea there was usually an increase in the stools of both dietary and non-dietary fat. The sources of non-dietary fat were from bile, the breakdown of cells, and intestinal synthesis. Professor Frazer described the chemical and radiological methods employed to assess small-intestine function.

The sprue syndrome, which included those cases of steatorrhoea without a gross intestinal lesion, comprised coeliac disease, tropical sprue, and non-tropical sprue. In Birmingham 30 cases of coeliac disease had been treated by the gluten-free diet, and all but two children were cured of symptoms, though the latent defect might remain. Gluten was present in wheat and rye flour and probably a peptide fraction was responsible. The crucial diagnostic test was the occurrence of relapse on a gluten-containing diet. Tropical sprue occurred among young, healthy, well-fed soldiers in Hong Kong within eight weeks of their arrival. There was definite improvement with folic acid therapy (15 mg. daily), but in some patients the small intestine did not return to full health. There must be some local factor which conditioned the deficiency of folic acid, but this remained undiscovered. In the treatment of idiopathic steatorrhoea it had been found that about half the cases responded to a gluten-free diet maintained for some months. In the remainder no cause had yet been discovered.

Secondary Steatorrhoea

Dr. D. G. CAMERON (Montreal), in discussing secondary steatorrhoea, described only that variety which followed operations on the gastro-intestinal tract. Patients presented with one or more of the following conditions: weight loss, unexplained megaloblastic anaemia, iron-deficiency anaemia, and osteomalacia. The steatorrhoea, which was sometimes not clinically apparent, was disclosed by balance studies. In his series of seven patients the sex incidence of six males to one female could be explained by the fact that the steatorrhoea followed an operation for duodenal ulcer in six cases (subtotal gastrectomy in five). The seventh patient had a colonic cul-de-sac following resection of the lower ileum and anastomosis to the transverse colon. In all the cases substantial improvement followed treatment. The megaloblastic anaemia was corrected by folic acid, by vitamin B_{12}, or by liver extract, and the iron-deficiency anaemia responded well to iron. Diarrhoea was controlled by moderate restriction of fat and the osteomalacia by calcium lactate and vitamin D. Weight was gained by all the patients, but none regained their pre-operative weight.

Post-menopausal Osteoporosis

Dr. A. W. BAGNALL (Vancouver) gave an account of post-menopausal osteoporosis. He accepted Fuller Albright's description of osteoporosis as a decreased production of osteoid by osteoblasts associated with a deficiency of the protein matrix mass, with a secondary deficit of the mineral mass. Anabolic activity was decreased or inhibited, while catabolic activity was normal. The only substances known which controlled protein deposit in bone were oestrogens and the androgens, while corticosteroids would increase the catabolism of protein in bone as in other tissues. The clinical features of the condition included a "dowager's hump," narrowing of the distance between costal margin and iliac crest, and back pain. It was emphasized that there was never spinal-cord or nerve-root compression with neurological signs. This was most useful in differential diagnosis from other conditions causing crush fracture of the spine. In addition to lessened density and crush fractures, radiological examination of the spine showed

coarsening of trabeculae and expansion of the disk. Another unexplained sign was the increased rapidity of the sedimentation rate.

In treatment 2 pints of milk should be ordered together with 2 dr. of calcium lactate daily, a high-protein diet, and 50,000 units of calciferol. Immobilization was to be avoided, but an orthopaedic support and a non-sagging bed were useful. Dr. Bagnall used oestrogens and androgens together, and without interruption, in therapy. The results were satisfactory.

Pyelonephritis in Diabetics

Dr. G. E. JORON (Montreal) called attention to the condition of acute pyelonephritis occurring in diabetics. Pyelonephritis had long been recognized as part of the nephropathic picture in diabetes, but Dr. Joron was particularly concerned with the fact that the pathologist not uncommonly found in diabetic patients that an unsuspected acute pyelonephritis had been the cause of death. He concluded from this that recognition of acute pyelonephritis might be difficult in the diabetic, and he analysed 23 cases in order to clarify the diagnostic difficulties. Only three of these patients had pain in the loin and only two had tenderness there. The patients as a group were much more ill than could be explained by the physical findings. A further cause of difficulty was that pus might not be identified in the urine. This could be due to bladder atony in these elderly diabetics, so that a relatively clear supernatant urine was voided. One cause of this relaxed bladder might be a diabetic neuropathy.

If the diagnosis was suspected, repeated examination of a catheter specimen of urine must be made and the urine cultured. Diabetic ketosis and acute abdominal lesions had to be considered in the differential diagnosis. Chloramphenicol (2 to 4 g. daily for one week, and 1 to 2 g. daily for the second week) was usually an effective therapy. A severe secondary anaemia often occurred and required transfusion.

Thursday, June 23

Aetiology of Rheumatic Fever

In the absence of Sir HENRY COHEN (Liverpool), Dr. E. R. CULLINAN (London) presided over the final session of the Section of Medicine.

Dr. D. A. LONG (London), speaking on the aetiology of rheumatic fever, said that Group A streptococci provided the most important clue to the aetiology of rheumatic fever. Infection with haemolytic streptococci was followed during convalescence by an ill-defined diseased state (the post-streptococcal state of Rantz) which merged into the full rheumatic syndrome. Any known type of this organism could, after a delay of three weeks, initiate the disease. This complication occurred not during the acute stage of bacterial invasion and toxaemia, of adrenocortical stimulation and protein catabolism, but during the prolonged subsequent stage of repair, anabolism and—it was suggested—hyperinsulinism. Rheumatic fever occurred in hyperimmune children. The incidence was low in diabetics; conversely, according to some authorities, it was associated with hyperinsulinism. The presence of hypersensitivity of the tuberculin type to streptococcal allergens, together with an "allergic," not a "pyogenic," response on the part of the tissues, suggested that the disease was due to bacterial allergy. On the basis of experiments in guinea-pigs, Dr. Long suggested that haemolytic streptococci provide an exotoxin which acts synergistically with the allergen to produce damage, and which, in addition, converts a local to a systemic allergic response. A logical and convincing, if rather technical, criticism of the anaphylactic hypothesis followed.

Dr. Long selected, on the basis of topical interest, one of the many factors that influence the conversion of the post-streptococcal state to the rheumatic syndrome. After surveying Coburn's work on the prophylactic value of egg yolk and the separation, with the phospholipid fraction, of an anti-anaphylactic substance, he said that, in collaboration with Dr. A. J. P. Martin, a similar substance had been separated from peanut oil, and probably the same substance was concentrated in egg yolk. In very small doses it depressed sensitivity to tuberculin in guinea-pigs. Nevertheless, in Dr. Long's opinion, the antirheumatic activity of egg yolk was more likely to be due to essential amino-acids than to any anti-allergic substance present.

Physiological Disturbances in Emphysema

Dr. E. C. WARNER (London) said that pulmonary emphysema occurred in 3 to 5% of patients. Inspiration resulted after muscular action, expiration from passive elastic recoil of the lung. Emphysema was due to loss of pulmonary elastic tissue secondary to chronic bronchial obstruction, repeated coughing against a closed glottis, and—possibly—bronchial arteritis. The latter required further study.

Loss of pulmonary elasticity and, therefore, of passive expiratory recoil was compensated for by an active muscular expiratory effort resulting in depression of the diaphragm, the so-called "paradoxical movement." Distension of the lungs caused a two- to threefold increase in residual air at the expense of vital capacity, over-ventilation of some areas of lung, and under-ventilation of others. The exact location of the latter was unknown. Experiments with helium and carbon monoxide showed that this space was largely excluded from normal respiratory exchanges and had a poor blood supply. Deficient ventilation resulted in a decreased tension of oxygen and retention in blood and alveolar air of carbon dioxide, resulting respectively in polycythaemia and an increased bicarbonate reserve in the blood. Once anoxia developed, tissue respiration was maintained by increased cardiac output resulting in hypertrophy of heart muscle.

Treatment of Emphysema

Dr. T. H. AARON (Edmonton, Alberta) undertook a high-speed review of all aspects of the treatment of chronic pulmonary emphysema, including an appraisal of mechanical aids to breathing and of various drugs which are still in the experimental stage.

In general, irritants and allergens should be excluded from the respiratory tract, and infection should be treated with the appropriate antibiotic. The airway must be cleared of mucus by the combined use of expectorants, aerosols of various types, and humid air. At the same time the airway should be enlarged by relieving bronchial spasm: ephedrine, aminophylline, and cortisone all had this effect. Various mechanical aids were illustrated and described. Pressure breathing and oxygen therapy were briefly discussed, and the treatment of associated heart failure considered along orthodox lines.

Investigation of the Haemorrhagic Diatheses

Dr. WILLIAM I. MORSE (Boston) reviewed the physiology of clotting, brightly illustrating his remarks by means of drawings of pin men in "comic-strip" fashion. He then went on to consider the haemorrhagic disorders in terms of disturbed physiology. Thus, deficiency of fibrinogen occurred congenitally, and it was associated with liver disease, with pregnancy, or with incompatible blood transfusions. Deficiency of prothrombin might also be congenital or occur with liver disease, with deficiency of vitamin K; in addition, various drugs—for example, dicoumarol—might cause it. In haemophilia there was deficiency of the antihaemophilic factor. Platelet deficiency could be divided into thrombocytopathic purpura (qualitative change in platelets) and thrombocytopenic purpura (quantitative change in platelets). The latter might be due to disease of bone marrow, of spleen, or of liver; to injections; and to drugs. Idiopathic thrombocytopenic purpura also occurred. Vascular defects associated with scurvy, uraemia, infection, heart disease, anaphylaxis, and as part of various syndromes caused purpura.

The diagnosis could be made by combining a careful history (details of family history and diet were important) with thorough physical examination, including tests for capillary fragility, and with laboratory investigation. Simple but valuable laboratory tests were blood smear, estimations

of haemoglobin and white blood cells, bleeding time, clotting time, and tests for clot retraction. Complex but important tests were those for prothrombin time, prothrombin consumption, estimations of fibrinogen, and platelet counts.

Treatment of Hyperthyroidism

Dr. JOHN P. GEMMELL (Winnipeg) said that the choice of treatment in hyperthyroidism was between surgical and non-surgical, but the results obtained by either method must be assessed by comparison with those obtained in untreated cases. Of these, 60% underwent natural remission, 20% improved, 5% failed to improve, and 8% died.

Pre-operative treatment consisted of 100 mg. of propylthiouracil given four times in the day. After three weeks iodide therapy was added. At six to eight weeks surgery could be undertaken. Agranulocytosis occurred in 0.2% of patients, the incidence being unrelated to the dose of propylthiouracil. All patients were warned to report either fever or sore throat immediately they occurred. Surgical treatment cured 85% of patients, myxoedema occurred in 5–10%, and in 5% the disease recurred. One per cent. developed vocal palsy, 1% tetany, and 0.5% died.

Non-surgical measures had to compete with these results. One hundred and one patients, divided into three groups—nodular, diffuse, and recurrent—were treated with radioactive iodine: 81 responded successfully, 17 became hypothyroid (chiefly older patients and those in whom the disease had recurred), 2 were uncontrolled, and 1 failed to respond. No fixed rule for deciding the dose of radio-iodine could be given, for many factors had to be considered. A theoretical drawback to this type of treatment was the possibility of inducing carcinoma.

Surgical treatment was indicated in patients under 40 years of age with diffuse toxic goitre and for all patients with adenomatous goitre. Radio-iodine was valuable for the treatment of recurrences at any age, for diffuse toxic goitre in patients over 40 years of age, and when surgery was excluded for other reasons.

In reply to a question, Dr. Gemmell said that no one method had obvious advantages over another in the treatment of malignant exophthalmos.

The chairman, Dr. E. R. CULLINAN (London), in concluding the final meeting of the Section of Medicine, thanked all speakers for their communications. He expressed the gratitude of all to Dr. R. C. Dickson (Toronto) for the skill and immense amount of quiet work that he had devoted to making this section a success. Finally, speaking for visitors from Britain, he expressed gratitude for their kind reception, for invitations to speak, and for the grace with which they had been heard.

SECTION OF OBSTETRICS AND GYNAECOLOGY

Thursday, June 23

Breech Delivery

With Mr. JOHN PEEL (London) in the chair, Dr. F. L. JOHNSON (Hamilton) described his method of breech extraction. He believed that the maternal soft parts caused difficulty in breech delivery more often than all other causes combined. In particular, difficulty was most often due to attempting delivery before full dilatation of the cervix, or to the presence of a very tense lower uterine segment. The latter must be relaxed by deep anaesthesia before extraction was commenced. Close co-operation between obstetrician and anaesthetist could do much to reduce the foetal loss. In the five years ending in 1954, 593 primary breech presentations had been delivered with a corrected foetal mortality of under 1%.

Dr. Johnson then detailed his technique. With the patient in the lithotomy position, early episiotomy was performed. If the legs were extended, they were brought down without necessarily waiting for their descent into the pelvis. The shoulders and arms were delivered by a rotatory manœuvre, and until this stage was completed no suprapubic pressure was applied. The aftercoming head was usually extracted by Piper forceps. He concluded by affirming that, above all, the steps of the extraction must not be hurried.

Functional Uterine Haemorrhage

Miss GLADYS HILL (London) read a paper on functional uterine haemorrhage, which she defined as abnormally frequent or excessive menstruation for which no cause could be found clinically or on curettage. Her procedure was to take a detailed history with special reference to psychological upsets, make a systematic clinical examination, and take vaginal cell smears. If the cause was not by then evident, curettage was performed and the material obtained was examined histologically. Cases could thus be classified into four groups. The menorrhagia of puberty showed low hormonal levels but with an oestrin preponderance. The cases in the 20–30-year age group manifested low hormone levels with no such preponderance. The disturbance of the later reproductive phase was marked by a hyperplastic endometrium, but the smears might show either some progesterone effect or only a high oestrin level. Menorrhagia at the climacteric gave a smear showing reduced hormonal levels with an oestrin preponderance.

These groups, said Miss Hill, were not clear-cut, but the classification had proved useful in deciding the place for symptomatic, surgical, radiotherapeutic, or hormonal treatment in the individual case. In particular, vaginal smears might provide a rational basis in hormone therapy for determining the exact form of treatment and for assessing its results.

Early Diagnosis of Cervical Cancer

Dr. D. M. LOW (Toronto) took over the chair when Dr. J. P. A. LATOUR (Montreal) discussed the early diagnosis of cancer of the cervix. He said that, in spite of arguments for and against, most gynaecologists now accepted the concept of the gradual progression over a period of years of carcinoma-in-situ to clinical cancer. It was therefore important to find the most efficient method of making the diagnosis of pre-invasive cancer. Tissue biopsy of the cervix was the oldest method but suffered the defect that the site of biopsy was taken at random unless a whole ring of tissue were removed. He doubted whether Schiller's test or colposcopy was very helpful in indicating the site for biopsy. The best method lay in examining smears from the cervix, for which purpose he preferred Ayre's method of scraping the cervix with a wooden spatula. The considerable variations recorded by different observers in false-positive and false-negative readings were due to the personal factor in reading the smears.

A positive smear, said Dr. Latour, required histological confirmation before treatment was undertaken, and ring biopsy with multiple serial sections offered the best chances of confirmation. Among 21,895 women screened, 375 had positive smears although cancer was suspected clinically in only 36. In all, 145 cases of carcinoma-in-situ were discovered. In 73% of 107 cases with positive smears, but clinically innocent cervices, subjected to ring biopsy, pre-invasive or early invasive cancers were found. No case of cancer was found in 34 women whose smears were negative but in whom the cervix looked suspicious enough to warrant ring biopsy. Dr. Latour concluded his beautifully illustrated presentation by saying that this most valuable diagnostic method had now become generally available since smears could be mailed in from outlying districts to an established cytology centre.

Cancer Education

After Dr. Low had vacated the chair in favour of Dr. W. P. TEW (London, Ontario) Mr. MALCOLM DONALDSON (London) discussed the value of cancer education. He said that in relation to carcinoma cervicis the education of women to consult their doctor at the earliest possible moment was a greater problem than the actual diagnosis of the condition. The outstanding symptom was irregular vaginal bleeding, but, as this was often transient or believed

to be due to a simple cause, women were not easily persuaded to regard it seriously. It was particularly important to correct this attitude in women over 40 years of age. The way would thus be clear towards cutting down the delay between first appearance of symptoms and first medical consultation. This in turn would probably result in a higher proportion of cancers being diagnosed in the earlier stages when treatment gave better results. Paradoxically, when the delay extended beyond six months the prognosis again improved. This was presumably because of a larger proportion of cases being of the less rapidly growing type, the most malignant having already proved fatal.

Mr. Donaldson said that a pilot experiment in cancer education of the public in Yorkshire had produced encouraging results. He thought it a better line of approach than periodic routine examinations. This was because the small numbers of unsuspected cancers discovered by the latter method did not justify the expenditure of the relatively enormous amount of time by doctors and technicians. Nevertheless he believed that the screening of cases of cervical cancer by cytological smears was a most valuable aid to early diagnosis.

Obstetric Anuria

Professor DAVID STEWART (Kingston, Jamaica) described "The Treatment of the Suppression of Urine associated with Pre-eclampsia and Eclampsia." He had seen six such cases in 18 months, giving a high incidence among 1,518 deliveries in that time. In five of the six women a sudden and prolonged fall in blood pressure might have been the initiating factor in causing the anuria or oliguria. One of of the patients had died from eclampsia, but the other five recovered after conservative treatment on the Bull regime. The principle of this regime was to tide the patient over until kidney function returned. The features therefore included the careful control of water balance, and the administration of sufficient carbohydrate to minimize protein metabolism and the release of potassium from the cells. In addition anaemia must be treated, infection prevented or controlled, and electrolyte imbalance, especially of potassium, sodium, and bicarbonate, corrected. If the required amount of fluid could not be taken by intragastric drip, it was given intravenously, if necessary into the superior or inferior vena cava by way of a polythene catheter.

At each of the four stages of the condition—onset, anuric phase, and early and late diuretic phases—it was convenient, said Professor Stewart, to have facilities for blood electrolyte estimations. However, the principles of treatment were simple enough to allow most cases to be treated adequately in the absence of such facilities, provided that the clinical course of the illness was closely observed.

SECTION OF RADIOLOGY

Wednesday, June 22

DIAGNOSIS

Under the chairmanship of the vice-presidents, Dr. JOHN WILKIE (Sheffield) and Dr. A. C. SINGLETON (Toronto), five papers were given on widely separate topics.

Diodrast Arthrography of the Knee

Dr. L. R. HARNICK (Toronto) summarized his experience of diodrast arthrography of the knee in over 500 cases. Accurate visualization of medial and lateral meniscus lesions was obtained by a scrupulous technique which included directing the *x*-ray beam parallel to the joint surface. The procedure, which was carried out in the *x*-ray department, involved injection of the dye through the lateral aspect of the joint after removing the effusion. The procedure was painless and was followed by only a minor degree of effusion in all but a few cases. No infection followed, and there was no inflammatory reaction seen histologically.

It was possible to visualize and to classify the types of injuries of medial and lateral meniscus, those of the medial meniscus being 12 times as common. Dr. Harnick had been able to check the roentgenographic diagnosis by the subsequent surgical exploration of 164 cases, in which the diagnosis was found to be correct in 93%.

Intracranial Calcifications

Dr. JOHN WILKIE (Sheffield) classified intracranial calcifications into physiological, non-neoplastic, and neoplastic groups. The physiological group were symptomless, but a calcification in the pineal body could be of use in indicating space-occupying lesions. The pathological but non-neoplastic group included the vascular degenerations, such as arteriosclerosis and aneurysm. Angiomatous malformations were generally superficial and could be associated with an external angioma, as described by Weber. Of the inflammatory lesions, cured cases of tuberculous meningitis might show calcification, usually at the base of the skull. With the increasing survival rate in cases of cerebral tuberculosis, calcification due to this cause may become much more important in the future. A high frequency of calcification was seen in parasitic diseases such as toxoplasmosis, less in cysticercosis. Symmetrical calcification in basal ganglia occurred in hypoparathyroidism.

About 15% of all intracranial tumours showed calcification, most frequently occurring in the craniopharyngioma and meningioma.

Duodenal Ulcer

Dr. R. A. MACPHERSON (Winnipeg) commented on the increasing demand being made on roentgenological services as an outcome of the greater use of prepaid health plans. As a result of this duodenal ulcers were now encountered at an early stage when symptoms were slight. He emphasized the importance of diagnosing duodenal ulceration that did not show associated deformity of the bulb. The work was based on 106 such early cases, representing 5% of his total cases of clinically active ulcers. The early cases were rarely found in hospital patients.

Diagnosis was largely based on pressure-spot films of the duodenal bulb using varying degrees of compression. These views demonstrated ulcers with a definite crater and, in many cases, a large cap. No deformity of the bulb was apparent, and without these specific films the diagnosis might have been missed. The cases showed the usual age distribution and symptoms of duodenal ulcer; the symptoms had frequently been of extremely short duration.

The speaker felt that a large atonic cap was of significance both in preventing the appearance of deformity and possibly in causing the ulcer. A questioner asked whether the large cap antedated the ulcer or was caused by it. Dr. Macpherson had the impression that large bulbs predisposed to ulcer formation. Another speaker remarked that in his experience large caps did not predispose to ulcer. The chairman, Dr. WILKIE, inquired into the method of getting adequate compression in cases with a high transverse stomach. Dr. MACPHERSON replied that these were difficult cases and that in some the diagnosis might be missed. It was, however, in the large atonic stomach that most value could be obtained from the method.

Ureteral Block and Kidney Function

Dr. G. GILL (Montreal) discussed the effect of ureteric block on the function of the kidney. Seventy-five cases with ureteric obstructions were encountered in the course of 943 intravenous urography examinations, and 40% of the cases with calculi had caused a blockage of the ureteral passage such that renal function could be threatened. The symptom of pain ought to be correctly interpreted: while the relief of pain in most cases was due to elimination of the calculus or a decrease in ureteric block, the pain relief may be a sequel to the silent loss of kidney function. When obstruction was recent the surgical removal of the obstacle reestablished the mechanical function of the ureter and the physiological function of kidney. Dr. Gill believed that there was little hope of recuperation of renal function in ureteral obstructions of long standing when urography failed

to visualize the collecting system above the obstacle; he felt that surgical operation was then useless. He also stressed the identical effects of extrinsic compression of the ureter.

Dr. MACPHERSON inquired for how long radiographs should be taken before coming to a decision about loss of kidney function. Dr. GILL felt that this depended on the size of the obstruction. If it was large, the case was a surgical emergency and excretion studies should not be pursued. The CHAIRMAN asked about the methods quoted in determining pelvic and ureteric pressures which would induce pain. Increased pressure in the kidney pelvis was the main cause of pain. Dr. GILL quoted the work of Risholm, who found that this symptom could be produced by a relatively low pressure (33 mg. Hg) in the kidney pelvis, yet a pressure in the lower part of the ureter of over 150 mm. Hg failed to produce pain. The degree of pain depended on the site of obstruction. The speaker stressed that this was true so long as the renal function was sufficient to keep up the pressure.

Forward Dislocation of the Atlas

Dr. D. G. WOLLIN (Toronto) presented details of eight cases of forward dislocation of the atlas. There were no deaths. Details of an experiment were given to substantiate the radiographic picures in these cases. Two patients showed evidence of cord compression, four had associated congenital bony abnormalities. The aetiology of the displacement was not established. The speaker believed that the condition was abnormal, and secondary to disease or defect of the transverse ligaments of the atlas.

Dr. KRUGER (Woodstock, Ontario) described a case which he had seen in which the ligament had been torn for one year, after which there was a final fatal rupture.

Thursday, June 23

Radiotherapy

With the president, Dr. J. RALSTON PATERSON (Manchester), in the chair, five papers were given.

Dr. ETHLYN TRAPP (Vancouver) described the physical characteristics of the woman with carcinoma of the uterine body. Metabolic disorders, obesity, delayed menopause, and hypertension were commonly associated conditions. Dr. Trapp's remarks about the role of radiotherapy at all stages of the disease were based on a study of 149 treated cases. In the earliest stage (stage 0) radiotherapy was used in patients who were poor surgical risks. In stage 1 it was indicated for poor surgical risks and for anaplastic disease: it was the treatment of choice, as advocated by Heyman, who used intracavitary radium. It could be used in conjunction with surgery either pre-operatively as a "planned" technique or post-operatively in the more advanced case, and also as a prophylactic measure in the surgically treated case to prevent metastases in the vaginal scar. In the stage 2 cases full radiation treatment aiming at cure was now possible in a much larger number of cases because of the advent of supervoltage radiation, including cobalt-60. In the incurable case useful palliation could be achieved.

In the discussion Dr. J. BOUCHARD (Montreal) asked what percentage of cases developed metastases in the vaginal wall. Dr. TRAPP replied that the figure was about 10%. The CHAIRMAN observed that it was questionable whether this figure justified prophylactic irradiation in all cases. Dr. TRAPP felt the procedure was justified. A dose of 6,000–7,000 r was delivered at the site of the scar and was applied not only as a prophylactic measure but as part of the planned treatment.

Malignant Tumours of Brain

Dr. J. BOUCHARD (Montreal) discussed the roentgen therapy of over 400 tumours treated by Dr. Carleton Peirce and himself during a 15-year period. The criteria of benefit included the length of survival and the ability to return to useful life. Over 300 of the cases were gliomata, and 57% of these survived twelve or more months. In a breakdown of this diverse group it was found that patients with glioblastoma multiforme had the shortest survival time. The astrocytoma group treated by combined surgery and irradiation showed much better results. Nearly as good results were obtained in a pathologically unclassifiable group of gliomas. Smaller numbers of such tumours as ependymomas, oligodendrogliomas, spongioblastomas, and haemangioblastomas were reported, the results of radiotherapy being reasonably good. Of the 46 cases of medulloblastoma, about one-quarter had a fair probability of living five years after treatment and of playing a useful part during that time. After the astrocytomas, this was the most favourable group. Dr. Bouchard was confident that the prognosis was good in meningeal tumours, although he could not give five-year survival figures. Of the pituitary adenomas (41 cases) the most satisfactory response occurred in the chromophobe type—78% of the patients being able to resume normal life compared with 50% of those with eosinophilic lesions. No adverse effects due to irradiation of the pituitary in the course of treatment of intracranial lesions had been seen.

Dr. L. V. MACDONALD (Edmonton) asked whether preoperative irradiation of chromophobe adenomas predisposed to bleeding. Dr. BOUCHARD replied that most cases were treated by radiation alone. He had not encountered bleeding in cases treated post-operatively; however, he allowed a six-weeks delay between surgery and radiotherapy and used small initial doses of radiation. A questioner asked if pneumoradiographic studies were done to assess recovery of the patient. Dr. BOUCHARD replied that this had been done in some cases, and in medulloblastomas recovery could appear complete. In a reply to a question by the CHAIRMAN, Dr. BOUCHARD said he gave 4,000 r to 4,500 r in a course extending over 40–50 days as the treatment for chromophobe tumours.

Bladder Cancer

Dr. R. C. BURR (Kingston, Ontario) summarized the work done jointly with Dr. W. E. Berry on the treament of bladder cancer. He felt that for the early and superficial tumour surgery was preferable. When the tumours were multiple or infiltrating, intracavitary radium had advantages. This included implantation of radium or radon, the insertion of a cobalt or radium source, and the use of radioactive solutions in direct contact with the bladder wall. In the infiltrating lesion which was definitely beyond surgical treatment the decision lay between total cystectomy and irradiation, the latter method including radium or radon implantation or the use of cobalt sources supplemented by external radiation. Supervoltage radiation through several ports or by rotation produced the most favourable results in the late case.

Dr. C. H. A. WALTON (Winnipeg) and the CHAIRMAN both commented on the rising numbers of cases being referred for radiotherapy as the good results were becoming apparent.

Leukaemia

Dr. EDITH PATERSON (Manchester) spoke on the incidence and management of the leukaemias. She described the rising incidence in England during the last 15 years. A comparison of the age distribution of leukaemia in Great Britain, Canada, and the U.S.A. showed that the greatest increase had occurred in men in the older age groups in Canada and in the U.S.A. This was not true for malignant disease taken as a whole. Leukaemia therefore constituted a greater fraction of the total incidence of malignant disease in Canada and in the U.S.A. In England the incidence was higher in men in the professional than in other social classes. Dr. Paterson urged that research should be applied to studying those social and geographic factors which might account for the differences in incidence.

An account was given of the present-day methods of treatment compared with the results of splenic irradiation. These included the method of use of ^{32}P as it was practised in Manchester, and the use of chemotherapeutic compounds such as urethane, "myleran," and triethylene-melamine. In acute leukaemia full use of the antimetabolite compounds

offered the best palliative treatment. In acute monocytic leukaemia, 6-mercaptopurine was sometimes of value.

Radioactive Gold in Malignant Disease

Dr. OWEN B. MILLAR (Toronto) gave the results of instilling ^{198}Au into the pleural or peritoneal cavity in 100 cases of advanced malignant disease. Patients were considered to be improved if either no further aspirations were required or the frequency of aspirations was drastically reduced. Dr. Millar described his ingenious technique. The best results were in carcinoma of the breast, the chest instillations being successful in 50% of the cases. Results of abdominal installations were not so good. In 16 patients in whom the primary site was unknown improvement occurred after 50% of the treatments. Of the miscellaneous cases it was disappointing that lymphomas showed little response. The gold injections took some time to act and should not be used on very ill patients. The use of post-injection scanning to indicate loculation of fluid was recommended.

Dr. WALTON (Winnipeg) commented that he had obtained a good palliative result with radiogold in a case of pseudomyxoma peritonei, using hyaluronidase. In a reply to a question, Dr. MILLAR said that if a patient responded once he was likely to respond to a second instillation; conversely, a non-responding patient should not be treated again.

SECTION OF DERMATOLOGY

Wednesday, June 22

Whitfield Tradition

With the president, Dr. R. M. B. MACKENNA (London), in the chair, and before an audience of over 200 members, Dr. D. I. WILLIAMS (London) read a paper on the Whitfield tradition of therapy. This tradition, he said, was still passed on to-day by senior colleagues in the old department where he worked. The difficulties of treating fungous infections of the skin were well understood by Arthur Whitfield, and he stressed the need for strict attention to detail in removing thick horny skin before applying local treatment. Sterilization of socks and towels was needed.

Psoriasis was next considered in some detail, and the speaker pointed out that Whitfield liked internal remedies such as arsenic and intestinal antiseptics in the treatment of this disease. The treatment of warts by 3% formalin solution in a small bottle held upside down on the wart for 10 minutes twice daily produced useful results, but the wart should be prepared by paring down the skin first.

Pruritus ani was another troublesome complaint, and contact with water was best avoided here. Camphor had its place in the relieving of severe irritation and could be used in a strength of 2% with menthol 1% in a zinc cream.

Dr. BRITAIN SANDERS (Toronto) gave an account of the investigation and treatment of 476 cases of ringworm of the scalp seen in children between the ages of 2 and 15 during the years 1949–53. Most cases occurred in the age group between 5 and 11, and there was an incidence of seven males to one female in the series. The majority of these were caused by *Microsporon audouini* infection. Some variation in the appearance of fluorescence of the hairs had been noted; it seemed to become less marked as the disease diminished. *X*-ray epilation was the treatment of choice, and the Kienböck–Adamson fine-field technique was used. Cultures carried out in 209 patients showed an incidence of 86% with *M. audouini* infection. The area where clippers were used by the hairdresser was involved in 55% of these patients. When examination by Wood's light showed no fluorescence of hairs, children were allowed to return to school. Out of 272 patients, 86% were back in school within six weeks.

In the discussion which followed, points which were stressed were that cultures and microscopical examination should be carried out in cases of persistent scurfy patches of the scalp, and that children should be excluded from school once a positive diagnosis had been established.

Rosacea

Dr. B. USHER (Montreal) gave an interesting short paper on the aetiology of rosacea. He admitted that many causes contributed to the establishment of this disease, but himself thought it was a manifestation of a general vascular disturbance with presenting signs on the face. Gastroscopic examination showed varying degrees of change in the gastric mucosa which could be correlated with the facial appearances. Chronic gastritis, atrophy of the mucosa, and even ulceration could be seen in some cases. Excellent illustrations of these were shown.

Dr. R. MASON BOLAM (Newcastle-upon-Tyne), in a paper on acute skin diseases in general practice, pointed out the changing nature of superficial infections of the skin since the introduction of chemotherapy and antibiotic substances. Penicillin-resistant organisms were on the increase. Schemes of treatment were outlined for impetigo, acute infected seborrhoeic dermatitis, and severe contact dermatitis. The use of simple remedies such as wet compresses, rest in bed, and adequate sedation all had their place, and a daily intravenous injection of 10 ml. of a 10% solution of calcium gluconate could be shown to limit exudation and swelling.

Illustrations were shown of many acute skin diseases such as bullous erythema multiforme, orf, and granuloma pyogenica, as well as examples of contact dermatitis, with patch-test results.

SECTION OF UROLOGY

Wednesday, June 22

Bladder-neck Disease

With the president, Mr. H. P. WINSBURY-WHITE (London), in the chair, a number of papers were read on various subjects. Mr. Winsbury-White spoke on "The Early Stages of Bladder-neck Disease," which he claimed was more common than was generally appreciated. In 500 cases in which bladder-neck obstruction had been relieved by open operation there was clinical evidence of fibrous change in 31%. Chronic inflammation had been confirmed by histological examination in a similar series of cases, none of which had been treated with an indwelling catheter. Chronic inflammatory changes had also been demonstrated in 274 patients suffering from chronic frequency of micturition. The aetiology in both sexes was probably much the same except for the extra hazard of child-bearing in women. Chronic inflammation could be demonstrated by urethroscopy in many women, and similar changes could be seen in childhood. Laboratory examination of the urine was seldom helpful, but on intravenous pyelography an abnormality in the ureters and kidneys could sometimes be discovered. Definite residual urine was found in quite a number of patients of both sexes over the age of 50. Mr. Winsbury-White concluded by showing that in the treatment of chronic urinary infections it was well to consider the urethra as a possible source of trouble.

Management of Genito-urinary Disease by the G.P.

Dr. JOHN K. LATTIMER (New York) then discussed the role of the general practitioner in the treatment of genito-urinary tuberculosis. Symptoms generally occurred relatively late in the disease, and the presence of small numbers of pus cells was an important sign. The majority of cases occurred in the third decade, but some presented for the first time much later in life. Epididymitis was the first clue in 60% of men with this type of tuberculosis. In establishing the diagnosis, the importance of both culture and guinea-pig inoculation was stressed. Continuing to discuss the investigation of these cases, Dr. Lattimer mentioned the possibility of *x*-ray changes, and pointed out that in the mild cases with small lesions the pyelogram was commonly normal. Treatment with antibiotics had greatly altered the picture of this disease. With treatment for periods of at least one year, the urine would often become sterile. This

had occurred in some 39% of those treated with streptomycin alone, in 60% of those treated with isoniazid, and in 93% of those treated with streptomycin and P.A.S. But combinations of all three drugs had rendered the urine sterile in 100% of cases, though relapse was bound to occur in some with the passage of time. Treatment with the antibiotics had facilitated a much more conservative surgical policy, and many patients for whom a nephrectomy had formerly been done were now left with their kidneys. During treatment intravenous pyelograms were done every three months to ensure that stenosis of the ureter was not taking place. So far as bladder disease was concerned, this generally responded well, but fibrous contraction of the bladder occurred in 10% of cases. There had also been a considerable reduction in mortality from kidney disease, and, with good judgment, the more conservative approach of surgeons had given very good results.

The Ileum in Genito-urinary Surgery

Mr. LESLIE N. PYRAH (Leeds) spoke about the use of the ileum in genito-urinary surgery. This operation had been done in some 23 patients for a variety of reasons: in 7 cases to enlarge a contracted bladder; in 3 to replace a ureter; in 3 to enlarge a healed and contracted tuberculous bladder and to correct an associated hydronephrosis in the one remaining kidney; in 2 to re-implant ureters which had previously been transplanted to the colon; in 6 to act as an artificial bladder; and in 2 cases to replace an excised bladder. Mr. Pyrah said the method he used was to isolate a segment of the terminal ileum and carry out side-to-side anastomosis to the bladder. The operation was invariably borne well, but there were sometimes difficulties with micturition for a month or two. Since the ileum could contract, it did not act like a diverticulum, and therefore did not become infected. The urine was usually sterile after the operation and the cystoscopic appearance satisfactory. In the pre-operative preparation of these cases 250 mg. of chlortetracycline was given four-hourly for four days. So far, the patients who had had this operation were faring well, but it was as yet too early to assess its final place in treatment.

Haematuria

Mr. A. W. BADENOCH (London), in discussing haematuria, said this was a symptom which should never be ignored, and he went on to describe the differential diagnosis of the various common conditions which could give rise to this trouble. Haematuria with abdominal pain was nearly always due to a stone, but the symptomless variety was most often due to neoplasm. The importance of full clinical assessment, with rectal and bimanual examination of the bladder under anaesthesia, was stressed. Most renal tumours could be demonstrated by urography. An aortogram might occasionally be helpful in distinguishing a cyst from a neoplasm. There remained a small group of cases in which the exact cause could not be found. In some of these the blood came from both kidneys, due to hypertension, congenital polycystic disease of the kidneys, nephrosis or nephritis, or to some blood disorder. In haematuria of unilateral origin without obvious cause, rather more than one-half had an angioma which might be so small that it could only be demonstrated after nephrectomy. However, such conditions were uncommon, and the commonest cause of haematuria was bladder neoplasm, which was responsible for some 60% of painless bleeding. Finally, Mr. Badenoch stated that bleeding from the prostate, though not uncommon, must be assumed only when all other lesions had been eliminated.

Vesical Neoplasms

Mr. NOEL ADENEY (Bournemouth) completed the programme with a discussion of vesical neoplasms from the provincial surgeon's point of view. He dealt briefly with the special problems which confront a general surgeon in dealing with common bladder tumours. He described the various problems concerned in diagnosis, and especially in differentiating benign from malignant tumours, and then discussed the problems of treatment by surgery and irradiation.

SECTION OF OTOLARYNGOLOGY

Wednesday, June 22

Facial Palsy

Mr. T. E. CAWTHORNE (London) presented his paper from the chair as a joint production of himself and Dr. D. R. HAYNES, of Johannesburg. He pointed out that the facial nerve fits so tightly into the Fallopian canal that even the smallest amount of swelling produces an interruption of the nervous impulse. In an analysis of his cases, Bell's palsy was found to be the commonest cause and injury next commonest. With regard to Bell's palsy, he thought that the causation was still in doubt, and he pointed out that, where the paralysis is complete, recovery without operation could be expected in only 42% of cases. Where it was incomplete, the expectation of recovery was 82%. He thought that an estimation of recoverability by electrical tests was unsatisfactory, because a positive answer might be obtained only when it was too late to operate. The decision to operate might be a difficult one, but operation in less hopeful cases might lead to symmetry of the face while at rest. With cases of nerves injured at operation, he noted that the incus was sometimes dislocated at the same time, so that where there was evidence of this having occurred there was a clear indication for operation. He drew attention to diminished lacrimation in lesions of the geniculate ganglion. With regard to clonic facial spasm, he had decompressed 13 nerves in such cases and found no visible pathological lesion. Some of these patients had recovered.

Dr. JOSEPH SULLIVAN (Toronto), opening the discussion, agreed with the diagnostic point on the dislocation of the incus and praised the point made about diminished lacrimation in geniculate ganglion cases. In cases of chronic spasm he recommended the removal of one-half to one inch (1.3 to 2.5 cm.) of the nerve, and its reinsertion back to front as a graft.

Dr. W. J. MCNALLY (Montreal), Mr. J. P. A. FINDLAY (Sydney, N.S.W.), and Dr. S. W ALLISON (Boston) took part in the discussion.

Treatment of Oesophageal Varices in Portal Hypertension with Sclerosing Injections

Mr. RONALD MACBETH (Oxford) noted that portal hypertension could be intrinsic to liver disease, or extrinsic owing to thrombosis of the portal vein or a main radicle. In both types of cases the most troublesome symptom was haematemesis from rupture of the oesophageal varices. In intrinsic cases that was usually due to liver failure. In extrinsic cases death from haemorrhage was rare, but the incapacity of haematemesis was considerable.

Treatment must be aimed solely at relief of haemorrhage. The only veins at risk were those prolapsing into the lumen of the oesophagus. Other deeper veins were in fact forming a useful function. Sclerosing injections, using sodium morrhuate 5%, could control such varices indefinitely in extrinsic cases and for limited periods in intrinsic. But oesophagoscopy once or twice a year must be continued. Splenectomy should be carried out as an adjunct. Experience with 30 cases suggested that the method was a safe and satisfactory alternative to major surgery.

Dr. PERCY IRELAND (Toronto), in opening the discussion, said he thought that the mortality rate of the shunt operation was probably lower than had been stated. He emphasized the possible value of the injection technique as emergency treatment.

Dr. G. E. TREMBLE (Montreal), Dr. S. L. ALEXANDER (Toronto), Dr. G. A. HENRY (Toronto), and Dr. T. J. MOLONEY (Toronto) took part in the discussion.

Observations of Respiratory Cilia with the Electron Microscope

Dr. G. E. TREMBLE (Montreal) said that although cilia may appear to be homogeneous extensions of a cell, they were in fact complex structures. The electron microscope had revealed that in lower animals and in man the cilia showed an axial core consisting of a number of paired fibrils within a sheath. One cell may carry as many as a thousand cilia. The length of a cilium was 67 microns, or about the size of a red blood corpuscle. The axial core was imbedded in a basal body. He noted that the structure of the tails of spermatozoa was almost exactly similar. He said that the exciting influence of the beat of cilia and flagella was completely unknown. He showed a short film to illustrate his points.

Dr. ANGUS CAMPBELL (Toronto), in opening the discussion, gave an appreciation of the value of the electron microscope and noted, as a practical point, that nasal mucous membrane had some power of rejuvenation.

Dr. ALLISON (Boston) and Mr. V. E. NEGUS (London) took part in the discussion.

Parotid Tumours

Dr. HOWARD MCCART (Toronto) said that otolaryngologists should pay attention to the parotid gland and other salivary glands; not only did they exhibit interesting pathology, but the parotid formed the bed of the extra-mastoid part of the facial nerve. He described the section of the nerve through the gland tissue, and noted that it lay between a larger superficial and a smaller deep lobe. He found electrode stimulation valuable in the exploration. He reviewed common and uncommon swellings of the parotid, and reminded his audience that suppuration in the gland was a difficult problem for treatment. In this connexion surgery should be avoided as long as possible and suitable antibiotics preferred. Mixed salivary tumours should be removed extracapsularly, and frank malignancies might need a total parotidectomy.

Dr. PERCY IRELAND (Toronto), in opening the discussion, emphasized that the salivary glands were suitable for consideration by otolaryngologists, but that proper training in their treatment was needed.

Dr. F. MONTREUIL (Montreal) showed a series of colour photographs of parotid swellings, and emphasized the importance of chest *x*-ray films in such cases.

Dr. J. SULLIVAN (Toronto), Mr. V. E. NEGUS (London), Dr. J. K. BRYDON SMITH (Toronto), Dr. ALLISON (Boston), and Dr. W. J. MCNALLY (Montreal) took part in the discussion.

SECTION OF ANAESTHESIA

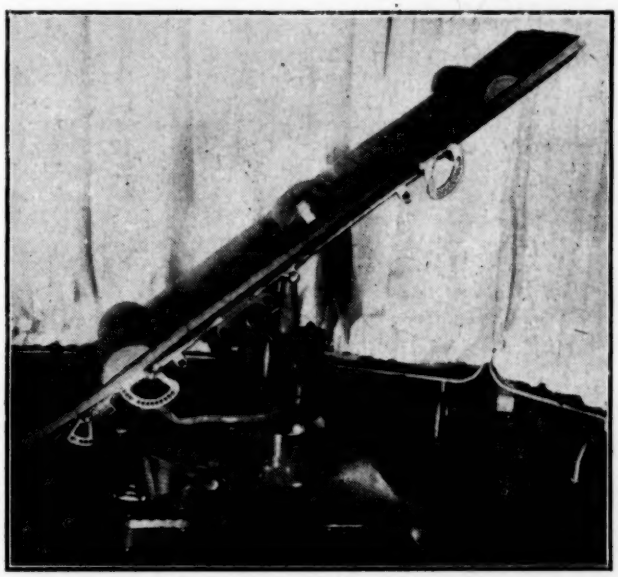
Wednesday, June 22

The Trendelenburg Position

The meetings of the Section of Anaesthesia were held at the Banting Institute. At the meeting on Wednesday, June 22, Sir ROBERT MACINTOSH (Oxford) occupied the chair. Dr. C. LANGTON HEWER (London) opened with a paper on "The Physiology and Complications of the Trendelenburg Position." This position, which was not first described by Trendelenburg, had been used, he said, for 70 years to make the interior of the pelvis accessible by displacing its movable contents into the upper abdomen. Patients commonly operated on in this position were middle aged, seldom healthy, and had poor vasomotor control. In healthy conscious adults there was little change in blood pressure and pulse rate, but in anaesthetized patients the blood pressure at heart level rose. The blood pressure rose progressively from the foot, where it might be 80 mm. Hg systolic, to 120 mm. at heart level, and 150 mm. in the head. There was approximately a rise of 20 mm. for every inch (2.5 cm.) vertically above heart level.

While the Trendelenburg position might be beneficial for a short time in the treatment of shock, it could be harmful in the elderly poor-risk patient; cerebral haemorrhage could result. After the operation the table should be levelled slowly to restore vasomotor control gradually. The pressure of the abdominal contents on the diaphragm displaced the latter and compressed the lungs, with a significant decrease in vital capacity. Hypoxia and hypercarbia were likely to occur unless steps were taken to prevent them. The rise in carbon dioxide tension was directly proportional to the angle of tilt. If the colon was distended with gas, the passage of a stomach tube and the complete emptying of the stomach might make more room for it. Gastric juice, saliva, and mucus tended to collect in the nasopharynx, and should be aspirated with a suction catheter in case they were inhaled.

Now that adequate abdominal relaxation could be obtained by the use of the muscle relaxants, Dr. Hewer thought there was seldom any need for the Trendelenburg position. If it were used the tilt should only be slight and not 45°. If it was necessary to put a patient in this position, care should be taken in maintaining it. Bending and strapping the legs could produce thrombosis and pulmonary embolism, and the use of shoulder rests might result in brachial plexus palsy, particularly if the arm were abducted as well. Dr. Hewer then described his method of maintaining the patient in position by skin friction, using a corrugated rubber mattress hooked on to the foot of the table (see Fig.). This with three transverse corrugated bolsters to fit the concavities of the neck, back, and legs prevented slipping, particularly if the patient's back was uncovered.



Anaesthesia in the Future

Dr. H. R. GRIFFITH (Montreal) took a look into the future when he discussed "Whither Now in Anaesthesia?" He said that he had seen vast changes in the last thirty-five years. What did the future hold? He thought that the training of the anaesthetist would be considerably improved. Knowledge would no longer be acquired by trial and error and by sitting at the foot of the master. The aim should be to train good clinical anaesthetists, not scientists; the scientist was of great help in advancing the frontiers of anaesthesia, but his training and background should be different. There would be increased attention paid to securing pulmonary ventilation and the removal of carbon dioxide. Some mechanical device, with a positive as well as negative phase, was needed to maintain ventilation in long operations. It should also be capable of manual control in

case of mechanical failure. Dr. Griffith visualized the increased use of gases in anaesthesia because they were more controllable in use and relatively non-toxic. They did not upset the metabolic processes like the barbiturates. One of the gases, with a muscle relaxant, could be used for almost any operation. He considered cyclopropane to be the most useful anaesthetic gas; it was safe, efficient, and liked by the patient. He thought that there might be a revival in the use of ethylene, and a decreased use of intravenous agents, particularly the barbiturates. The latter should be used only in small doses to induce sleep and not as true anaesthetic agents. Dr. Griffith said that he saw no great future for chlorpromazine in anaesthesia. He referred to the use of "viadril," a steroid, which was a good basal anaesthetic agent, and to "dolotral," which might replace thiopentone. Discussing local analgesics, he said that the old ones were still the best. Referring to the use of muscle relaxants, he disagreed with those who taught that they were dangerous. Used intelligently, with skill, with careful attention to dosage, and with controlled respiration, they were relatively safe. Succinylcholine was a particularly safe relaxant because it was rapidly hydrolysed.

Dr. Griffith said that cardiac arrest should become increasingly rare with more skilled anaesthetists in charge of the patient, but it was likely to occur with the more daring surgery of the future. The use of spinal anaesthesia would continue, he said, in spite of the possibility of complications. However, these could be minimized by using the less toxic drugs, diluting them well, and calculating the dose carefully. With regard to hypothermia, he thought that it would have no future unless safer drugs were discovered. At present it should be reserved for cardiac surgery. The anaesthetist of the future, said Dr. Griffith, must be a physician, a pharmacologist, a physiologist, a biochemist, an electronic engineer, and a toxicologist.

Antidotes to Muscle Relaxants

Dr. A. R. HUNTER (Manchester) described antidotes to curarizing drugs. There were species variations in their action, so that information obtained from any one animal could not necessarily be applied to man. Anaesthetists also had different techniques in administering relaxant drugs; some produced a greater degree of myoneural block than others. Tests on animals employing the head-drop technique or the dropping of a mouse off a revolving drum were not altogether satisfactory, as they did not measure the relaxation of the diaphragm, and this was the only danger in man. Antidotes to depolarizing myoneural-blockers acted by competition and had a chemical structure similar to that of the drug they were blocking. Thus hexa- and pentamethonium reversed the action of decamethonium. Dr. Hunter referred to a compound known as 49-204 that also blocked decamethonium. Fortunately most depolarizing myoneural-blocking agents were so short-acting that antidotes were rarely necessary. Antidotes to competitive blocking agents either increased the amount of acetylcholine reaching the end-plate or increased the responsiveness of the end-plate to the small amount of this substance that passed the barrier created by the blocker. Neostigmine possessed both these actions, but it might fail in cases of extreme myoneural block, and also occasionally after ordinary doses of curarizing drugs. In large doses it produced a myoneural block itself, and it also had a muscarinic action. Dr. Hunter described a compound known as 51-212 that antagonized both depolarizing myoneural-blockers and competitive blockers, but owing to its depressor action its clinical use was not recommended. The organic phosphates and physostigmine were of little use. "Tensilon" and "mestinon" resembled neostigmine structurally and pharmacologically, but they had less muscarinic action.

Part of the confusion concerning the value of the antidotes to muscle relaxants had arisen because some anaesthetists used them to restore normal breathing, while others sought complete restoration of function of all the muscles. More powerful antagonists were required for this and they tended to produce unwanted muscarinic actions.

New Intubation Technique for Lung Surgery

A new technique of intubation for the prevention of contralateral infection during lung surgery was described by Dr. L. LONGTIN (Montreal). He described the use of two separate cuffed tubes in the bronchial tree delivering anaesthetic gases to each lung. One was in the left bronchus and delivered gas to the left lung. By blowing up the cuff the left bronchus could be sealed off. The other tube was in the trachea 2 cm. below the vocal cords and delivered gas to the right lung as the left was sealed off. Both tubes were connected to the same gas machine. Succinylcholine was used to relax the patient. Sir ROBERT MACINTOSH said that he had been working along similar lines and demonstrated tubes that he was using.

Anaesthesia in Children and Infants

Dr. R. W. COPE (London) discussed anaesthesia in children and the newborn, with special reference to abdominal and plastic surgery. For abdominal surgery, except in emergencies, "omnopon"-scopolamine, or oral barbiturates and atropine were given for premedication. Induction of anaesthesia was most commonly completed with intravenous thiopentone followed by nitrous oxide, oxygen, and ether or cyclopropane. Muscle relaxants pushed to the stage of complete curarization were used during the maintenance of anaesthesia. Oral intubation with an uncuffed tube was done after relaxation with succinylcholine. Intermittent intravenous pethidine was sometimes used in a dose of 0.5 mg. per lb. (1.1 mg. per kg.) of body weight to produce sensory depression. For neonatal emergencies an endotracheal tube was passed under direct vision while conscious. Then the calculated dose of D-tubocurarine chloride (2 mg. per stone (0.3 mg. per kg.) body weight) was injected and artificial ventilation carried out, first with oxygen and then with a mixture of oxygen and nitrous oxide in equal volumes. As abdominal tone returned small increments of D-tubocurarine were given. No other drugs were used. It was fatally easy to overhydrate babies with intravenous or subcutaneous fluids. These should be limited to 10 ml. per stone (1.6 mg. per kg.) body weight in 24 hours. Babies and children often required repeated operations for the repair of congenital and acquired deformities. Premedication was with omnopon-scopolamine followed by intravenous thiopentone, or rectal thiopentone, 1 g. per 50 lb. (44 mg. per kg.) body weight in a 2.5% aqueous solution. Chlorpromazine and promethazine were used for post-operative sedation. Dr. Cope also referred to the use of hypnosis in the anaesthesia of young children. In children undergoing plastic surgery controlled hypotension was sometimes necessary. This was achieved with hexamethonium bromide.

Assessment of Post-operative Analgesics

Dr. P. R. BROMAGE (Chichester) described a new method for the assessment of analgesics based on the restoration of respiratory function under conditions where breathing was restricted by post-operative pain. The vital capacity was reduced by 60 to 80% during the first 48 hours after an upper abdominal operation. This reduction was caused by pain and was measurable by spirometry. Complete regional analgesia restored the vital capacity to normal. Hence the potency of an analgesic could be expressed as the amount by which it restored the vital capacity. Drugs under test were administered to a series of patients in the immediate post-operative period and the maximum percentage restoration of vital capacity measured in each case. Using this method a regional nerve block gave the best results. Methadone was slightly better than pethidine in degree of relief and duration. Intravenous lignocaine was inferior to both these analgesics.

Thursday, June 23

Chlorpromazine

With Dr. B. C. LEECH (Regina) in the chair, Dr. D. A. BUXTON HOPKIN (London) reviewed the position of chlorpromazine in anaesthesia, based on its use in over 2,000 cases. He said that a mixture of 50 mg. each of chlorpromazine,

promethazine, and pethidine given one hour before operation and repeated just before the operation reduced anaesthetic resistance. No atropine was given. Both promethazine and chlorpromazine exerted a selective depression on the subcortical centres and took the patient half-way to surgical anaesthesia. They had no hypnotic action, which was supplied by an intravenous barbiturate. Nor did they produce analgesia, but this was achieved with nitrous oxide and supplementary pethidine. Long operations could now be done using only an intravenous barbiturate and nitrous oxide as the anaesthetic agents. There was no need for powerful volatile anaesthetics with the mixture described. Recovery, however, could be prolonged, as these drugs intensified the action of anaesthetics. In the presence of chlorpromazine ether exerted a cardiac depressant action, and as chlorpromazine reduced peritoneal reflex irritability and muscle tone the dose of muscle relaxants, if used, should be reduced. The duration of action of the latter was not, however, prolonged. Operative shock was absent after using chlorpromazine, even in the presence of prolonged and traumatic radical surgery. There was no shock or fall in blood pressure after peritoneal traction if the patient had received the drug. Hypotension sometimes occurred, particularly in the elderly, but chlorpromazine was not contraindicated in haemorrhagic shock if blood was given as well. The signs of shock in a patient with a perforated viscus could be reversed by the intravenous injection of the chlorpromazine mixture. After a small dose of an intravenous barbiturate and a muscle relaxant, the patient was prepared for surgery.

Dr. Hopkin was impressed with the excellent condition of the patients post-operatively; pulmonary complications were reduced and there was less vomiting and coughing. Restless, senile, and uncooperative patients became calm after operation. Indeed, chlorpromazine with a little pethidine was a useful post-operative sedative. Dr. Hopkin said that he had not seen jaundice in any of his patients, as this complication occurred only after the continued use of the drug.

In the dosage used in anaesthesia chlorpromazine exerted two significant pharmacological actions—a peripheral adrenolytic action, and a central depressant action which could be demonstrated by the electroencephalograph. There was no convincing evidence that hypothermia was essential for the drug to exert its effect during anaesthesia. Although chlorpromazine caused deepening of respiration when given alone, it could reverse apnoea due to pethidine. Many of the actions of chlorpromazine could be explained by its depressive action on what is known as the reticular activating system of the brain stem.

Progress in Anaesthesia

Dr. H. J. SHIELDS (Toronto) gave a scholarly account of the history of anaesthesia in Canada, based on his own examination of the literature. He said that in 1847 Nelson, of Montreal, experimented with ether and used it in the removal of a thigh tumour within a few months of Morton's work on the subject in Boston. In 1848 chloroform was used for the first time in Canada by Holmes, only three months after Simpson's use of it in obstetrics in Edinburgh. By the middle of the century ether and chloroform were in widespread use in Canada as anaesthetics. Dr. Shields paid respect to Dr. Wesley Bourne as one of the pioneers in the teaching of anaesthesia in Canada during the present century. He was the first secretary of the Canadian Association of Anaesthetists, incorporated in 1920, and was the first recipient of the Hickman medal. There were other Canadian pioneers in anaesthesia. The use of cyclopropane was first suggested by Dr. G. H. W. Lucas; ethylene was being used for the first time in Canada while it was being tested in the United States; Dr. Harold Griffith, of Montreal, introduced curare into anaesthesia; and Dr. R. Gordon, of Toronto, was the first to use intravenous procaine for the relief of pain.

In a paper entitled "The Anaesthetic and the Anaesthetist," Dr. R. JARMAN (London) reviewed the progress made in the last hundred years in anaesthesia. After the pioneer work of Wells, Snow, and Simpson, chloroform, ether, and nitrous oxide were the only anaesthetic agents used for almost eighty years. Progress had been rapid since the first world war, and particularly during the last twenty years, which had witnessed the introduction of a wide range of intravenous and relaxant drugs. The anaesthetist himself had also entered a new phase. Once considered to be relatively unimportant and paid accordingly, he was now almost universally recognized as one with a training and a qualification matching those of the physician and surgeon, and one who should be consulted on the patient's condition and treatment before, during, and after the operation. Dr. Jarman paid tribute to the research on new drugs made by the leading pharmaceutical companies. He suggested that the research now carried out by anaesthetic departments and individual anaesthetists should be co-ordinated by a research centre in every country with a professor responsible for the final assessment. The attractions of research should not obscure the practical side and the human touch in anaesthesia.

As Dr. F. Hudon, of Quebec, was unable to present his communication, Sir ROBERT MACINTOSH demonstrated apparatus recently developed in his department at Oxford. He showed a development of the Oxford vaporizer which had inflating bellows so that controlled respiration could be performed with it. The machine was capable of delivering a given mixture of ether and air or other volatile anaesthetic, and the composition of the mixture was independent of the surrounding temperature. A 4% ether mixture was perfectly safe to use. He also demonstrated an improved intratracheal tube and intravenous needle.

Round Table Discussion

A round table discussion was held on Thursday, June 23, to discuss questions arising from the two previous sessions. Dr. B. C. LEECH (Regina) was moderator, and a panel of nine anaesthetists from Canada and Britain answered the questions. In reply to a question on the passage of muscle relaxants across the placental barrier, Dr. R. GORDON (Toronto) said that they did pass the barrier, but whether they affected the foetus or not depended on the concentration. They could be identified in the placental circulation. Both Dr. G. S. W. ORGANE (London) and Sir ROBERT MACINTOSH (Oxford) said that they had never seen an apnoeic infant delivered by caesarean section after the mother had a muscle relaxant. Questioned on the best anaesthetic to give for a version when the presenting part was engaged, Sir ROBERT said that he would use a small dose of thiopentone and a full dose of a muscle relaxant.

On the question of cardiac massage Dr. D. HUGGINS (Winnipeg) said that all equipment for this should be ready in the operating theatre and that every member of the surgical team, from the surgeon to the junior nurse, should have a definite function to fulfil. Valuable time was lost at the outset if the team was not organized. Dr. ORGANE said that if the massage was effective the finger-nails would turn pink. Dr. HEWER (London) said that the aorta should be squeezed at the same time as the heart was being massaged to raise the coronary pressure. Dr. LONGTIN (Montreal) said he had known cardiac massage to be kept going for 10 hours. There was no precise time for keeping on with it, as it depended on the cause of the cardiac arrest. Dr. LEECH said that no case should be abandoned so long as an effective circulation was being maintained. If the pulse could not be felt the heart was no longer pumping or no longer filling.

Dr. GORDON replied to a question on the functions of the anaesthetist during atomic warfare. He said that every doctor should be trained to give a simple anaesthetic, with lay assistants if necessary. There was no place for elaborate anaesthetic techniques. Improvisation would be necessary; for example, any tube of correct size could be used for intubation. With regard to supplies, there was the double problem of availability and transport. Anaesthesia would have to be planned using ether, chloroform, intravenous barbiturates, and possibly relaxants. Apparatus for inflation should be available.

Dr. LANGTON HEWER (London) said in reply to a question that the Trendelenburg position was no longer needed with muscle relaxants, as they allowed access to any part of the pelvis. If it were used the tilt should be small and the position should not be prolonged.

Dr. GRIFFITH (Montreal) did not consider the explosion hazard any greater with cyclopropane than with ether, and it was no more apt to cause bleeding than any other agent.

The indications for spinal anaesthesia had largely disappeared with the introduction of the muscle relaxants, explained Dr. G. M. WYANT (Saskatoon). It was still used in certain lower abdominal procedures, haemorrhoidectomy, and caesarean section. Sir ROBERT MACINTOSH said that he would give it to the patient who did not want to sleep. Dr. COPE (London) considered that spinal anaesthesia should be used only if all other forms of anaesthesia were contra-indicated.

Regarding the use of the anaesthetic recovery room, Dr. E. A. GAIN (Edmonton) said that as soon as the patient left the theatre he should remain in the recovery room in charge of trained nurses until conscious and able to speak, until the blood pressure was stabilized and respiration normal, and until haemorrhage, if any, ceased.

Dr. WYANT considered that premature babies should be resuscitated first without oxygen, and if that appeared necessary it should not be given in a concentration of more than 30% owing to the danger of retrolental fibroplasia.

SECTION OF NEUROLOGY

Wednesday, June 22

Multiple Sclerosis

With the president, Sir GEOFFREY JEFFERSON, in the chair, Dr. DOUGLAS MCALPINE (London) spoke on the diagnosis and treatment of multiple sclerosis. He emphasized the need to demonstrate multiple lesions. The gradual spread of plaques in, say, the posterior columns of the spinal cord was reflected in the spread of paraesthesiae. Careful history-taking was of paramount importance. Several factors might play a part in aetiology, and the prognosis was not always bad.

With Dr. GILBERT L. ADAMSON (Winnipeg) in the chair, Dr. J. G. GREENFIELD (London) gave an account of some delayed neurological sequelae of spinal anaesthesia. In some of these cases, he said, spastic paraplegia developed some weeks later. At necropsy degenerative changes were demonstrated in the pial arteries, and there was a severe degree of arachnoiditis. Experimental studies by Dr. Weston Hurst had demonstrated in monkeys that the intraspinal injection of a small quantity of detergent or antiseptic caused a similar lesion. The commonly used spinal anaesthetics seemed to be harmless.

Epilepsy of Late Onset

Dr. HELEN DIMSDALE (London), discussing epilepsy of late onset in the light of modern diagnostic procedures, reported 200 cases, in 52% of which no organic cause was found: 20% were due to tumour and 4% to angioma, and 18% were associated with cerebral atrophy. Careful clinical examination was of the greatest importance in the identification of organic brain disease. Of the special methods of investigation available pneumoencephalography was probably the most informative in these cases and should generally be the first to be made; an E.E.G. was also desirable.

Focal Epilepsy

With Dr. W. RITCHIE RUSSELL (Oxford) in the chair, Dr. WILDER PENFIELD (Montreal), giving some results of his unique experience on cortical excision in the treatment of focal epilepsy, said the nature of the cortical change leading to an epileptogenic focus was not known. This "focus" was a zone of cortex—an area of grey matter from which this abnormal activity developed. At operation visible abnormality was identified in 97% of cases in a recent series of 234 cases operated on between 1945 and 1950. There was a high proportion of cases of birth trauma, and the development of epilepsy was much delayed. The follow-up studies indicated that the results were excellent in 45%, good in 20%, and poor in 35% of cases.

Cervical Spondylosis

Mr. D. W. C. NORTHFIELD (London), speaking on the results of operative treatment of cervical spondylosis associated with myelopathy, said that in 26 out of 38 cases there were multiple disk lesions. The spinal cord changes tended to appear in the distribution of the anterior spinal artery. Spastic weakness of the lower limbs was the most common presenting symptom. Two-thirds of the patients were 40 to 60 years of age. The operative treatment was laminectomy. The ligamenta denticulata were removed, the intervertebral foramina were enlarged, and in three cases spinal fusion was performed. The results of operation were good in 21 cases, but post-operative treatment must aim at protecting the weakened spine, and a collar should be worn for several months.

SECTION OF CHILD HEALTH

Wednesday, June 22

Problems of Gastro-enteritis

With the vice-president, Professor WILFRID GAISFORD (Manchester), in the chair, Dr. FRANCES H. PRISSICK (Montreal) discussed the present concept of the aetiology of gastro-enteritis. From the bacteriologist's viewpoint the clinical syndrome ranged from mild diarrhoea, through enteritis associated with parenteral infections, to primary gastro-enteritis of undoubted infectivity. Several groups of micro-organisms had been implicated and suspected in this syndrome: (1) recognized specific pathogens (the salmonella and shigella); (2) *Staphylococcus pyogenes*; (3) specific serotypes of *E. coli*; (4) "borderline" enteric bacilli; and (5) commensals and viruses.

Aetiological Significance of Various Micro-organisms

Three broad criteria were suggested for use as a yardstick against which suspect micro-organisms might be measured. First, was the micro-organism in question found in the majority of patients and uncommon in healthy individuals? Secondly, would it, or its products, reproduce the disease or give rise to symptoms or lesions when introduced into new hosts? And, thirdly, were specific antibodies produced in the course of the disease and/or convalescence?

Salmonella and shigella had long been recognized as specific potential pathogens by these standards. Because of its ubiquity, *Staphylococcus pyogenes* was more difficult to place. Undoubtedly pathogenic, its significance in the gastro-intestinal tract was complicated by the production of enterotoxin by some strains. The toxin might give rise to gastro-enteritis-like symptoms. Feeding experiments in man and intravenous inoculation into kittens confirmed this. Lesions and specific antibody were known to be produced by staphylococcal haemolysins, but immunological studies with enterotoxin had been hindered, since it was a poor antibody producer and it had not been separated entirely from haemolysin. Whatever the mechanism might be it seemed reasonable to suppose that staphylococci were implicated in some cases of gastro-enteritis, whether primary, secondary, or complicating antibiotic therapy.

The evidence for the potential pathogenicity in the intestinal tract of specific serotypes of *E. coli* rested at present chiefly on epidemiological studies. Outbreaks of diarrhoea and vomiting in infant wards and nurseries had been attributed to any one of the serotypes O 26, O 55, O 111, and O 127, on the basis of their isolation, often in large numbers, from patients during epidemics (and in sporadic cases too), and the absence of salmonella and shigella from the faeces. Feeding experiments in adults had had moderate

success in producing symptoms of gastro-enteritis. Antibody in the form of agglutinins had been detected in the sera of patients, volunteers, and convalescents, with varying degrees of success and conflicting views.

Dr. Prissick then discussed the "borderline" enteric bacilli—including the paracolon, Bethesda, and Arizona groups. These intermediary forms were perplexing because they possessed antigens related to salmonella. Epidemiological evidence connecting them with outbreaks of food-poisoning was slight, and it would be helpful when they could be identified as exactly as could the serotypes of *E. coli*.

Commensals, sometimes suspected as causes of gastro-enteritis, when present in large numbers in cultures of faeces of infants and when accepted pathogens were absent, were the proteus group and *Pseudomonas aeruginosa*. Their possible significance should not be denied because of the present lack of evidence to the contrary.

There was still much speculation about the possible role of viruses as aetiological agents in epidemic gastro-enteritis. It had been suggested that they might operate in symbiosis with one or other of the suspect enteric bacilli.

Drugs and Antibiotics

Dr. B. E. SCHLESINGER (London) described the changes in therapy which had developed during the past thirty years, from the days of the meat broths, albumin water, bismuth, and kaolin to the insoluble sulphonamide derivatives and the latest antibiotics. These changes had evolved as a result of revised views about aetiology and a fuller realization of the importance of effective rehydration and the rectifying of the disordered blood chemistry occurring in infants suffering from severe gastro-enteritis.

Dr. Schlesinger had not found the insoluble sulphaguanidine and phthalylsulphathiazole to be of great use in salmonella and shigella infections, and preferred those chemotherapeutic drugs which acted systemically. In viral gastro-enteritis he had found aureomycin at least partially successful. He went on to discuss the various types of *E. coli* which might be considered pathogenic, and described the recent Medical Research Council's clinical trials in which aureomycin, chloramphenicol, and sulphadiazine were compared as remedies for the treatment of specific coliform enteritis. These trials showed in general that sulphadiazine was the most useful drug, and chloramphenicol the second best. Dr. Schlesinger concluded that antibiotics should always be given in severe gastro-enteritis, if only to combat associated parenteral infection, but that drug therapy should never take precedence over rehydration and the correction of biochemical disorder.

Fluid and Electrolyte Balance

Dr. W. W. PAYNE (London) described the steps which should be taken to correct changes of electrolyte balance, assuming that no biochemical facilities were available. When gastro-enteritis occurred there was a partial or complete cessation of salt and water intake and an extra loss of fluid in the stools and vomitus. The blood potassium would fall steadily as the condition became more severe. The chloride would rise and ultimately—by the use of cellular protein when the effect of starvation became evident—the blood urea would also rise.

In assessing the degree of disturbance in any given infant, the history would help, particularly that of the duration of the illness and the amount of weight lost. Clinical examination would confirm the degree of severity and dehydration. In mild cases a fluid intake of 2½ oz. per lb. per day (70 ml. per 0.5 kg.) should be maintained and the fluid should contain about 0.3% of electrolytes and 5% glucose. Common salt was the simplest electrolyte to use, and in mild cases was quite satisfactory. More severe cases required additional potassium, and a mixture containing two parts of sodium chloride and one part of potassium citrate made up as a 0.3% solution with 5% glucose should be given as soon as free flow of urine occurred—that is, following 12 to 24 hours of glucose-saline. When vomiting prevented the retention of an adequate amount of fluid parenteral administration became necessary. This might be subcutaneous; if hyaluronidase were added, 600 ml. might be given each 24 hours for several days to an infant weighing 10 lb. (4.5 kg.). More severe cases necessitated admission to hospital for intravenous infusion.

In the discussion following these three papers Dr. R. SOUTHBY (Melbourne) reported that there had been several epidemics of staphylococcal gastro-enteritis in infants in various States in Australia. He stressed the value of a nasal drip in the treatment of gastro-enteritis, and this was supported by Dr. A. GOLDBLOOM (Montreal), who also recalled the good prognostic omen presented by the onset of diuresis in any infant suffering from gastro-enteritis. Dr. G. M. KOMROWER (Manchester) remarked on the varying severity of *E. coli* infections, and questioned the aetiological significance of these organisms alone. Professor A. L. CHUTE (Toronto) said that he had seen an epidemic in infants in which *E. coli* O 11 had been grown in pure culture from the blood stream and also isolated at necropsy.

B.C.G. Vaccination in the Newborn

With the president, Professor ALAN MONCRIEFF (London), in the chair, Professor WILFRID GAISFORD (Manchester) described his experiences with B.C.G. vaccination in the newborn. He gave an account of the first five years' running of a B.C.G. clinic in which the particular interest has been in the vaccination of newborn infants, of whom some 6,000 (out of a total of 7,500 people of all ages attending the clinic) had been successfully vaccinated. He described the pros and cons of immunization in the newborn period and the complications encountered, together with methods of minimizing these. Variations in the type of vaccine used, and in dosage, had been studied, and Professor Gaisford discussed the effects of changes of temperature and of keeping the vaccine (up to eight weeks) on the viability of the organisms and on the vaccination results. He also outlined the methods and strengths of the post-vaccination tuberculin testing and the results obtained. Regular follow-up of the vaccinated infants had so far revealed only nine cases requiring re-vaccination. Of special importance had been the follow-up of infants born into tuberculous households, of whom there had been more than 500 known cases. As a result of this experience they had concluded in Manchester that vaccination against tuberculosis was a worth-while procedure in newborn infants, and with due safeguards merited an extended trial on a much wider basis than heretofore.

Bronchiectasis

Dr. GLADYS L. BOYD (Toronto) reported her results in dealing with 1,257 children referred for investigation for bronchiectasis. Seven hundred had bronchiectasis, and 650 of these had been followed sufficiently long for assessment. The three factors responsible for bronchiectasis were injury to the bronchial mucosa, obstruction in the lumina, and superimposed infection. The relationship of sinus infection to bronchiectasis was still debatable, but it appeared to be close in bilateral bronchiectasis, and treatment of the sinusitis was essential if successful treatment of the bronchiectasis was not to be nullified. Dr. Boyd considered bronchoscopy essential, and bronchography was carried out in all cases at the same time. Results of treatment had improved with better and earlier diagnosis and advances in surgical skill and experience. In 1930–5 there were 17 cases subjected to lobectomy, with seven deaths. In 1950–5 there were 28 cases, all cured. In 33 bilateral cases, bilateral resection was done in 21 and unilateral in 12. The results were better in the former. In those who had the double operation the more severely involved lobe was removed first to allow of possible regression in the other lung. Functional studies following resection were undertaken in 40 cases. Those in whom bilateral lower lobe resection had been performed showed the least disturbance.

Dr. A. W. FRANKLIN (London) considered that Dr. Boyd's results did not substantiate the necessity for surgery as a

curative measure, and stressed the dangers of bronchoscopic and bronchographic investigation and of operation. In reply to questions, Dr. BOYD said that she preferred bronchoscopy routinely before bronchography because it allowed of more complete clearance of the bronchi and subsequent visualization after "lipiodol" or "dionasil." She had encountered no damage to the larynx or trachea as a result of bronchoscopy.

SECTION OF PREVENTIVE MEDICINE

Wednesday, June 22

Combined Immunization

With the president, Professor L. P. GARROD (London), in the chair, a discussion on combined immunization was opened by Dr. H. J. PARISH (London), who presented the principles and practicable procedures for prophylactic immunization against smallpox, diphtheria, whooping-cough, tetanus, and tuberculosis at different ages from birth onwards. Antibody transferred via the placenta from mother to child could interfere with active immunization in early infancy, against diphtheria and smallpox, and perhaps against whooping-cough (though this was doubtful), but there was not this difficulty with tetanus (with a few exceptions) or tuberculosis. Vaccination against smallpox should be done first—around the third to fourth month of life when "alimentary equilibrium" was established, and preferably three weeks before any other immunization was begun. (In French Equatorial Africa smallpox and yellow-fever vaccinations by scarification were combined). Smallpox vaccination should be postponed if the child had any skin trouble or constitutional disturbance.

Early protection against whooping-cough was much to be desired, since most of the deaths occurred in the first year of life. Although combined immunization against this infection and diphtheria was not yet officially sponsored by the Ministry of Health, many local authorities were in fact using it. Tetanus toxoid could with advantage be included. The diphtheria–pertussis or triple antigens used in Britain did not contain alum, because of the possibly greater risk of post-inoculation poliomyelitis with "adsorbed toxoid." A large dose (25 Lf) of diphtheria toxoid should be combined with 20,000m. of *H. pertussis* and 5 Lf of tetanus toxoid; three injections at four-weekly intervals were given *subcutaneously* from the third or fourth month of life. Immunization with pertussis-containing antigens might have to be suspended in an area where poliomyelitis was occurring, but the available evidence incriminated particularly the alum-containing mixtures.

There was no contraindication to the active immunization of allergic children, although it was prudent to begin with a small dose. B.C.G. vaccination in infancy was recommended only for contacts and should be done some weeks after smallpox vaccination. Dr. Parish wondered if there might be "interference" with other immunizations if B.C.G. vaccine were given repeatedly. Where the triple antigen was used from the third month of life, a first booster could be given at 1 year of age.

The speaker then discussed the official immunization schemes of the U.S. Public Health Service and the British Ministry of Health. In Britain immunization against diphtheria with A.P.T. or P.T.A.P. was officially recommended when the infant was 8 to 12 months of age, partly to avoid the administrative problem of early booster doses, and partly because it was felt that if children were adequately protected in early life there was little chance of infection being carried from school or outside contacts into the home. For these reasons it was felt that combined diphtheria–pertussis immunization might also be deferred until the end of the first year. Dr. Parish suggested that as a compromise there should be a general "call up" of children at 1 year of age: those who had already had their primary immunization could be given a booster dose, while the others could be given their primary course. A permanent record card of inoculation was becoming essential. Booster doses might be given between 3 and 5 years of age, and certainly in diphtheria, with only about half the pre-school children immunized, primary courses or booster doses should be given to all children at school entry. A booster dose of pertussis vaccine at this age was undesirable. Combined diphtheria–tetanus toxoid, used as a booster for schoolchildren, might produce excessive diphtheria antitoxin and very little tetanus antitoxin if the children had already been immunized against diphtheria only. Finally, Dr. Parish reviewed the procedures for the combined immunization of adults in the armed Forces and in civilian life.

Canadian Experience

Dr. J. M. MATHER (Vancouver) reviewed his experience of combined immunizations in the Royal Canadian Air Force and in suburban counties in southern Ontario. With the disappearance of diphtheria, and whooping-cough rendered a mild disease after active immunization, mothers, while accepting the need for preventive inoculations, wanted the number of injections to be as few as possible. He favoured the triple antigen, for although tetanus was a rare disease it was safer to treat injuries entailing a risk of this infection with a booster dose of toxoid rather than with tetanus antitoxin. Besides, tetanus often followed minor injuries when antitoxin would not ordinarily be given. He felt that there was a shift in the incidence of whooping-cough, often in a mild form, to the schoolchild, and such children could infect very young siblings who had not been immunized. He would encourage booster doses of pertussis vaccine at school entry, and also wanted to see more immunization of adults against both diphtheria and tetanus.

Dr. P. J. MOLONEY (Toronto) dealt with some of the more academic immunological problems from the laboratory viewpoint. Among factors involved in the process of immunization were the variations in antibody response in a particular species, variation in the immunizing potency of different antigens, and the possible influence on the immunizing antigen of associated impurities. The great variation in guinea-pig response to diphtheria and tetanus toxoids (both efficient antigens) was well recognized, but so far unexplained: complete lack of response was unlikely to be due to agammaglobulinaemia. The relative efficiency of different antigens could be compared only if the equivalent amounts of antigen (in terms of antigen nitrogen) were injected into the same animals and the antibody produced also weighed. Under these conditions diphtheria and tetanus toxoid produced comparable results. Heterologous antigens could also be compared on the duration of immunity produced by them. Ordinarily the half-life of diphtheria antitoxin, measured in the infant with its maternally acquired antibody, was 20 days, and it was a fair assumption that the same held good for other antibodies. It was therefore likely that persistence of antibody following active immunization depended on the continuous production of antibody. In this respect tetanus toxoid was an extraordinarily good antigen, since it had recently been shown that useful levels of antitoxin were present ten years after the last injection. Associated impurities might affect the potency of an antigen either by stimulating or by suppressing production of the productive antibody, and Dr. Moloney illustrated this point by some results from the use of combined insulin and diphtheria toxoid. Again, purified toxoids were less likely to produce reactions in the inoculated than those with associated impurities.

In the general discussion, Professor R. CRUICKSHANK (London) presented some data from a controlled clinical trial of combined diphtheria–pertussis prophylactic compound with P.T.A.P. carried out at Barking, Essex, in association with his colleagues at the Wright–Fleming Institute. Combined diphtheria–pertussis antigens produced a better antitoxin response than A.P.T. had done in an earlier trial in infants of comparable age, while in slightly older infants P.T.A.P. gave a significantly higher antitoxin response than either of the other two.

In summing up, Dr. D. A. LONG (London) felt there was general agreement that combined antigens were desirable and could be more effective as immunizing agents than antigens used singly, particularly in the case of toxoids mixed with a bacterial vaccine. The soluble antigens, like the toxoids, were more effective than insoluble antigens. The immune response must be reassessed in relation to time and the number of injections. He did not favour assessment of antigens from the primary response, and suggested that the ability to condition cells to respond to secondary stimuli was the most important requirement in an antigen. There was no advantage in obtaining high antibody titres for adequate protection in the toxin-type infections.

SECTION OF ORTHOPAEDIC SURGERY

Thursday, June 23

Aetiology of Postural Defects

The second session held by this Section, with Dr. R. I. HARRIS (Toronto) in the chair, was devoted to further short papers. Mr. PHILIP WILES (London) described some psychological factors in the psychosomatic concept of posture, considering the visual, tactile, and proprioceptive impulses that contribute to Henry Mead's mental "schema" of the body image. This was part of the personality, and changed with growth. Normal posture, difficult to define, should satisfy mechanical and aesthetic demands; failure in these respects constituted abnormal posture—due either to mechanical defects or failure to adjust the schema during growth, often for emotional reasons. Treatment should conform to these causes.

Mr. DENIS BROWNE (London) then discussed the causation of certain congenital deformities and their treatment by controlled movement. He gave his reasons for supposing that some congenital deformities were caused by congenital abnormalities *in utero*—whether malposition, increased mechanical pressure, or increased hydraulic pressure. The supposition was based on obstetric histories, the correlation of various types of deformities, and the progress of deformity with growth. This group of deformities included talipes varus, metatarsus varus and valgus, and the irregular forms observed in spina bifida, some cases of congenital dislocation of the hip, congenital dislocation of the knee, congenital postural scoliosis (or idiopathic scoliosis), sternomastoid and congenital postural torticollis, and arthrogryposis. In treatment, classical methods of immobilization were less successful than "controlled movement," which was defined as the mechanical elimination of certain movements and the encouragement of others.

Malignant Tumours of Bone

Dr. L. P. ROY (Quebec) had surveyed all malignant bone tumours at l'Hôtel-Dieu, Quebec, over 10 years (1944–54). Of 97 cases, 20 were discarded as insufficiently documented or followed. Of 17 patients with multiple myelomata (8 male and 9 female, aet. 40–68), the 4 who had biopsy died in an average of 13 months, and those without biopsy in 14 months. All 7 patients (2 male and 5 female, aet. 20–51) with giant-cell tumours underwent biopsy and were alive and well at an average of 9.2 years after excisions followed by radiotherapy. Of 17 patients with osteosarcoma (8 male and 9 female, aet. 4–64), 7 operated upon died in 19.6 months and 8 without surgery died in 18.8 months; 2 boys aged 9 and 14, treated by amputation (after biopsy in one), were still alive and well after 10 years. The 3 patients (2 male and 1 female, aet. 10–47) with chondrosarcoma were treated surgically and were still alive after an average of 29 months. Of 12 patients with Ewing's tumour (6 male and 6 female, aet. 6–60), 9 treated surgically died in 18 months and 3 treated otherwise died in 19 months. Among 4 patients with fibrosarcoma (2 male and 2 female, aet. 8–68), 2 treated surgically were alive and well after 4 and 10 years, and 2 treated by radiotherapy died in 6 and 10 months. The survey included also 14 metastatic tumours. *X*-ray diagnosis was wrong or indefinite 24 times, biopsy twice. Biopsy appeared to be harmless.

External Pin Fixation

Discussing the complications of external pin fixation in orthopaedic surgery, Dr. F. P. PATTERSON (Vancouver) said that this treatment, revived in the last war, had been largely discarded because of the complications, sepsis being the most serious. Union had not appeared to be delayed in the cases in his hospital. The method, which was not easy, should not be used when conservative methods were suitable. It might be used in some cases of Bennett's fracture-dislocation, open fracture of the tibia and some very complicated injuries, and as an aid in some types of arthrodesis. It should be discontinued on the least sign of infection. Other complications included ischaemic necrosis of muscle and temporary paresis of the lateral popliteal nerve. In discussion, Mr. J. P. CAMPBELL (Nottingham) and Mr. H. H. LANGSTON (Winchester) mentioned the use of the method for the mandible, Dr. R. I. HARRIS (Toronto) for arthrodesis of the knee, and Dr. GEORGE PENNAL (Toronto) for Smith's fracture and certain difficult pelvic fractures. For general use, and especially in fractures of the femur, the method found no support by any speaker.

Discussing the feet and legs in childhood, Dr. G. L. BURKE (Vancouver) emphasized the importance of recognizing small signs of abnormality in infants, so that such conditions as congenital dislocation of the hip and metatarsus varus were treated in early infancy, when real cure was possible. Other abnormalities in the young, not to be neglected, were tightness of the medial rotators of the hips, tibial torsion, bow legs, and knock-knees, which often responded to simple treatment.

Dr. A. A. BUTLER (Montreal) discussed the theory of hydrocortone treatment in orthopaedics. It was more effective than cortisone, he said, in suppressing inflammatory manifestations. He gave the results of an average of three injections of 10–250 mg. of cortisone (average dose for a large joint 100 mg.) into 303 joints, including the large and small joints of the limbs, and of interligamentous spinal injections. The diseases for which treatment was given included osteoarthritis, rheumatoid arthritis, tendinitis, tenosynovitis, tendo-vaginitis, and bursitis. In each group most patients were improved, but a few were made worse.

Arthritis of Hip and Knee

In the treatment of osteoarthritis of the hip, Mr. J. P. CAMPBELL (Nottingham) considered that osteotomy deserved greater popularity. Internal fixation had widened its scope. Of 34 patients treated thus, one to five years before, 21 were completely relieved of pain, 9 had only an occasional ache, and 4 had residual pain. Hip movement was improved in 20, unaffected in 12, and worse in 2. At operation, deformities were corrected and the femoral shaft was displaced laterally by about half its thickness. Under *x*-ray control, a nail was inserted from the osteotomy site up the femoral neck over a guide wire and bolted to a plate screwed to the shaft; a further screw transfixed the fragments. No external fixation was used. After-treatment included bed exercises, pool exercises after three weeks, crutch walking after four, and discharge home with sticks after 6–8 weeks. Clinical and radiological evidence was shown suggesting some reversal of the arthritic process. Investigations in the engineering department of Nottingham University with photo-elastic materials had suggested that osteotomy abolished the lateral thrust on the humeral head by levelling the pelvis.

Discussing the surgical management of arthritis of the knee, Dr. R. GARIEPY (Montreal) said that now more rheumatoid than osteoarthritic knees came for reconstructive surgery. Synovectomy was preferably, but not necessarily, delayed until active progress was ended. Pre-operative treatment with cortisone or an ally was useful, and suitable doses did not interfere with healing. The synovial membrane was dissected bluntly, and the menisci and cruciate ligaments were preserved; patelloplasty had shown no advantage over patellectomy. Passive flexions were

carried out from the fourth day onwards. In traumatic arthritis, tibial and fibular osteotomies to correct valgus or varus might restore comfort; sometimes synovectomy would help. Arthroplasty gave promise in some carefully selected cases, but arthrodesis in slight flexion was reliable and useful. Established fixed flexion might respond to graduated manipulations, but high tibial osteoclasis or osteotomy was more certain and was preferred to capsulotomy, tendon lengthening, or prolonged traction.

Dr. J. N. SWANSON (Toronto) discussed some orthopaedic problems connected with gouty arthritis, and said that a distinction had recently been drawn between primary gout, in which the excess of uric acid was caused by faulty synthesis from glycine, ammonia, and carbon dioxide, and secondary gout caused by nucleic acid destruction in blood disease, such as polycythaemia rubra vera, leukaemia, myeloid metaplasia, and occasionally pernicious anaemia soon after liver therapy was started. His series comprised 160 primary cases and 8 possibly secondary. Gout had been confused clinically with cellulitis and arthritis, including that associated with psoriasis, especially when manifesting itself in joints other than that of the hallux. A history of previous attacks, familial disease, sudden onset, often at night, severe pain, diffuse and severe tenderness—these might all help in the diagnosis, besides the serum uric-acid estimation, perhaps joint aspiration, and the response to intravenous colchicine. Sometimes an independent condition called for operation in the gouty, occasionally on a joint. Attacks could usually be prevented by 0.6 mg. colchicine or 100 mg. phenylbutazone twice daily. In an acute attack, colchicine was customarily given intravenously in doses of 3 mg., repeated if necessary after eight hours. Alternatively phenylbutazone might be given, 600 mg. by mouth, followed next day by 100 mg. four-hourly, but its toxicity should be remembered. In chronic gout, "benemid" (which diminished renal tubule reabsorption of uric acid), colchicine, and phenylbutazone all might have a place.

SECTION OF PSYCHIATRY

Thursday, June 23

Basic Sciences in Psychiatry

With the president, Professor AUBREY LEWIS (London), in the chair, Dr. W. C. GIBSON (Vancouver) opened a symposium on the "Basic Sciences in Psychiatry" by discussing the contributions of physiology.

Dr. Gibson illustrated his theme by reviewing the researches in progress in his own laboratory. These included the silver staining of the unmyelinated fibre tracts from the frontal lobe in post-leucotomy brains; the researches of Dr. Margaret A. Kennard on the relation between E.E.G. findings and clinical psychological assessment of certain psychiatric syndromes, and also her studies on the interrelations between the frontal and temporal lobes in monkeys; the biochemical abnormalities in the urine of schizophrenics as demonstrated by paper chromatography; and finally the setting up of a large control series for his own studies of the finger-nail capillaries of patients on their first admission to mental hospitals. Dr. Gibson illustrated these latter findings with slides and raised their possible value in personnel selection.

Dr. A. DENIS LEIGH (London), discussing the contributions of neuro-anatomy and neuropathology, stressed the advances made during the last 20 years. The study of schizophrenia had contributed both directly and indirectly to the knowledge of brain anatomy, although in schizophrenia no neuropathological processes had been revealed. Leucotomy had thrown light on the functional and anatomical relationships between the frontal lobes and the basal ganglia and had contributed to the development of the concept of a "visceral brain." Again, studies of the temporal lobe and neurosurgical procedures had both practical value and theoretical interest in the elucidation of some of the problems of epilepsy.

Neuro-anatomy and neuropathology had also made a contribution to the study of ageing and of the presenile dementias. The development of histochemical techniques was full of promise and had helped in the understanding of some of the enzymatic processes of nervous tissue. Dr. Leigh concluded that neuro-anatomy and neurobiology had entered upon a new phase of usefulness in the study of psychiatric disorders.

Role of Consciousness

Dr. J. W. LOVETT-DOUST (Toronto) said that the divisions between medical psychology and clinical physiology had always been more apparent than real. To-day these twin sciences were profitably combined in psychophysiology, the scientific handmaiden of psychiatry.

The key psychological problem in psychiatry was that of consciousness. The whole edifice of Freudian psychoanalysis, and of its later psychodynamically orientated variants, was based upon the role played by consciousness in the genesis and maintenance of mental illness; descriptive and systematic psychiatry was confronted with the problems of the qualitative and quantitative aspects of awareness—from the stupor of the catatonic, through the convulsions, aurae, equivalents, and furor of the epileptic, the sleep disturbance of the depressive, to the thought disorder, hallucinations, and impaired attention and concentration of the schizophrenic. Forensic psychiatry constantly faced problems of consciousness with the alleged amnesias, fugue-states, and "blackouts" of delinquents.

The philosophical literature on consciousness was enormous: contributions from psychophysiology had only recently begun to appear. It was Dr. Lovett-Doust's contention that certain aspects of being conscious were susceptible to scientific investigation, and even to measurement. Over the past six years he and his co-workers had endeavoured to show how consciousness, if considered as the aggregate of a number of parameters of awareness, might be "quantified" by the use of psychophysiological "monitoring" devices, each of which changed in a direction and in temporal concordance with the clinically observable or subjectively reported awareness change of the patient.

Dr. Lovett-Doust gave illustrations of some of these monitors, with especial emphasis upon those concerned with minute capillary vascular anatomy and function. He suggested that effects of these changes would be seen and measured even at the level of the reversible pathology of the tissue cell, cytological changes of the nature of cloudy swelling and hydropic degeneration being observed at times of lessened attentive awareness and increased emotional awareness, and reversing as these aspects of consciousness reverted to their former status.

Psychobiology

Dr. W. C. M. SCOTT (Montreal) paid tribute to the psychobiology of Adolf Meyer, not least for having paved the way for the acceptance of Freudian metapsychology. The combination of psychobiology and metapsychology, now often called psychodynamics, was, however, faced with a twofold crisis—first, the amount of time involved before the student could obtain the requisite knowledge for treatment and research; and, secondly, the realization by psychiatrists of the growth of experimental psychology, mainly conducted by psychologists who were not medically qualified. The thesis put forward by Professor W. A. Hunt, that psychiatrists should accept the possibility of co-operating with and sponsoring non-medical psychologists, presented a challenge to psychiatrists of immense importance and significance. Psychological experience and concepts had in the past been mainly obtained from work in private practice. Further progress and verification might now be carried out in an institutionally subsidized setting, possibly under university auspices or helped by public money from governmental sources.

SECTION OF OCCUPATIONAL MEDICINE

Thursday, June 23

Health of the British Coalminer

With Dr. J. G. CUNNINGHAM (Toronto) in the chair, the president, Dr. JOHN ROGAN (London), discussed the health of the British coalminer since the National Coal Board was established in 1947. Although 750,000 workers, mostly miners employed in about 1,000 pits, were involved, comprehensive and comparable statistical data were hard to obtain. While it was still true that the mortality rate of miners compared unfavourably with those for all other men, there had been a steady reduction in it between 1911 and 1950, and the reduction was being maintained.

In 1951 the Registrar-General's Sickness Survey had shown that the miners lost through sickness twice as many days as all other groups. After briefly mentioning the commonest diseases of miners, Dr. Rogan discussed pneumoconiosis in some detail. Its exact prevalence was unknown, and the incidence varied greatly from mine to mine. In twelve mines, of the miners radiographed the percentages of those with simple and complicated pneumoconiosis had varied from 13 to 0.9, and 8.7 to 0.1, respectively. It was easy to define the conditions required to counter this hazard—namely, the reduction of dust to acceptable levels and the eradication of tuberculosis amongst the workers—but they were less easy to achieve. Amongst notable improvements in health had been a dramatic reduction in the incidence of miners' nystagmus, as a result of better lighting in the mines, and a steady fall in the death rate due to accidents since 1943, although the reported incidence of minor injuries had increased in 1948, when a revision of the compensation laws made it easier for benefits to be obtained. Absenteeism meant nothing on its own; the important thing was to know what was the reasonable attendance target for the mine in question.

A comprehensive medical service, consisting of 58 doctors and 268 nurses, had been built up by the Coal Board, and the main research effort was being directed against pneumoconiosis. It was important to define with some precision the quantity and quality of dust which could be safely allowed. In reply to a question, Dr. Rogan said that, although there had been a considerable improvement in living conditions in some mining areas, they were still deplorably bad in others and this undoubtedly contributed to some of the sickness incidence.

Plea for Regular Blood Sugar Examinations

In a brief communication, Dr. R. D. APPLEFORD (Hamilton) made a plea for the inclusion of blood sugar testing in the periodic examination of industrial workers. This would reveal occasional diabetics who would be missed if the urine alone were tested. In a recent survey, 108 of the older workers had blood sugar levels in excess of 150 mg.%. On further investigation, about half were considered to be diabetics of varying degrees of severity and in need of treatment. Several speakers were surprised at this high incidence, and Dr. J. H. BAILLIE (Toronto) said that, with urine testing alone, of 1,900 samples from employees of the Bell Telephone Company only 28 had given suspicious results, and of these only three were thought to be due to mild diabetes mellitus.

Bauxite-fume Pneumoconiosis

Dr. C. G. SHAVER (St. Catharines, Ontario) described 48 cases of bauxite-fume pneumoconiosis diagnosed between 1942 and 1946, of which 14 had proved fatal up to the present time. Furnace feeders and crane operators were mostly affected, usually after an exposure of 3 to 8 years. So far as he knew, no similar conditions had been reported before 1942. The clinical course was one of progressive fibrosis, complicated by spontaneous pneumothorax due to the rupture of subpleural emphysematous bullae. After the installation of an adequate ventilation system over each furnace, there had been no further cases. In reply to a questioner, Dr. Shaver said that the turnover of workers had been so rapid that it had been impracticable to calculate the incidence of this condition.

Health Hazards in the Oil Industry

Dr. S. D. MCCLEAN (London) outlined the various processes used in the oil industry throughout the world. Fire and hydrogen sulphide intoxication were prominent hazards, sulphuric acid and caustic soda were used in some processes, and the poisonous effects of tetraethyl lead were well known. Workers in contact with the last wore protective clothing and were kept under close medical supervision, blood counts being done routinely. Some carcinogenic chemicals were encountered, but shale-oil cancer, which was not uncommon 30 years ago, was to-day practically unknown, as the result of the men wearing better protective clothing and being more careful about their personal hygiene. After referring briefly to the possible hazards of radioactive isotopes which were used to test the quality of lubricating oils, and the wide variation in susceptibility to oil dermatitis, the speaker concluded by saying that the oil industry executives were well aware that it was a hazardous industry, and appreciated the need for an adequate medical service.

Air Hygiene in Warships

Surgeon Commander F. P. ELLIS (Royal Navy) said that in warship construction the need for meeting the requirements of material departments militated against the provision of optimum space for the men. The criteria for the latter were ill-defined. In warm climates the evidence available indicated that the "effective temperature" between decks should be kept below 78° F. (25.6° C.). In excessively warm situations the wet-bulb temperature provided a better guide, and even well-acclimatized, trained men would collapse after a few hours of moderate work if the wet-bulb temperature exceeded 92° F. (32.8° C.) when the dry-bulb lay between 100 and 110° F. (37.8 and 43.3° C.), or 88–89° F. (31.1–31.7° C.) when it was between 120 and 130° F. (48.9 and 54.4° C.), even when radiant heat was left out of consideration and the air was circulating briskly. Air-conditioning was essential for maintaining a ship in an operational condition if it had to be "closed down" for more than a few hours in tropical waters. In cooler latitudes a dry-bulb air temperature of 60–65° F. (15.6–18.3° C.) was preferred by the average man, and the more serious problem was to protect personnel against cold wind and wetness on the upper deck. Surgeon Commander Ellis also referred briefly to less prominent but important features such as insidious anoxia or rising partial pressures of carbon dioxide in closed-down ships and submarines, fluctuating atmospheric pressures in "schnorkelling" submarines, prolonged or repeated exposure to air with a high content of bacteria-carrying particles in crowded spaces, unpleasant odours generated by men's bodies, clothing, or the tobacco they smoked. He ended by discussing some of the principles affecting the control of atmospheric environment in enclosed spaces.

ROUND TABLE CONFERENCE

Tuesday, June 21

Prevention and Treatment of Poliomyelitis

With Dr. C. E. VAN ROOYEN (Toronto) in the chair, and a panel of experts—Mr. J. M. P. CLARK (Leeds), Drs. RITCHIE RUSSELL (Oxford), J. HILDES (Winnipeg), and W. T. MUSTARD, A. J. RHODES, and N. SILVERTHORNE (Toronto)—representing orthopaedic surgery, medicine, physiology, paediatrics, and virology, the good-sized hall was filled to overflowing for this question-and-answer session on the prevention and treatment of poliomyelitis. On the preventive side, the large amounts of vaccine used in the 1954 trial had been prepared in tissue cultures of monkey kidney plus the synthetic nutrient medium M.199 of Parker. The vaccines, which contained a small amount of penicillin

carried over from the production process, were tested for safety, sterility, etc., in three separate laboratories before being released. There had been practically no reactions to the injections, and the 129 cases of poliomyelitis which occurred among the 1½ million inoculated children within four weeks of the last injection were randomly distributed among those receiving vaccine or placebo, and there was no special localization of paralysis to the inoculated site.

The current programme for Canada was to inoculate subcutaneously the first three grades of schoolchildren (aged 6 to 8 years) with two doses of vaccine at four weeks' interval, to be followed by a booster dose one year later. So far, some 90% of the Canadian cases had been caused by type I virus, the vaccine of which had been least effective in the 1954 trial. This was thought to be due to the more destructive effect of " merthiolate," the preservative, on the type I antigen, and it was hoped that this drawback would be overcome this year. The question of the use of living avirulent vaccine by the oral route was raised, but there were numerous difficulties and problems still to be solved.

As regards treatment, while most cases could be adequately handled by experienced medical and nursing staff, some 20% required medical care by a team of experts with all the facilities of a general hospital. Transportation of severely paralysed cases could best be done by flying squads, which should include an anaesthetist with an oxygen outfit to give two pressures to help with suction and respiration and, if need be, a portable respirator. The patient as a first-aid measure should be nursed in the semi-prone position with frequent changes to right and left lateral, particularly if there was evidence of paralysis of respiratory muscles. On arrival at hospital patients with intercostal paralysis were placed in the tank respirator. For uncomplicated cases of bulbar paralysis a respirator must not be used: instead the patient should be nursed in the semi-prone position with suction and frequent postural drainage, and, if possible, a throat microphone so that the nurse could keep a sharp watch on his breathing. Tracheotomy was rarely needed. In patients with both bulbar and intercostal paralysis positive-pressure breathing through a cuff tracheotomy tube without a respirator (which allowed " chest-squeezing " by the physiotherapist during frequent changing of position) was recommended. General physiotherapy was not indicated during the acute stage, when paralysed limbs could be splinted to relieve pain. Ambulation should be begun not later than six months after onset, and tendon transplants could be used to correct deformities. Braces and similar appliances were useful as supports, but were not corrective. The panel felt that the advances in the control of poliomyelitis which might be expected within the next few years were more education of the public about poliomyelitis, more effective prophylactic vaccination, and the better prevention of limb shortening.

THE SCIENTIFIC EXHIBITION

The Scientific Exhibition at Toronto was on a comparatively small scale. The general standard was good, and the methods of displaying information were mainly on conventional lines. The sole British exhibit, on " Cancer of the Breast " from the Royal Marsden Hospital, did not suffer from comparison with any other presentation. The natural history, early diagnosis, and treatment, both radical and palliative, were clearly and graphically depicted. Other matters of surgical interest included a detailed exhibit from the universities of Illinois and Saskatchewan concerning the use of controlled hypotension in general surgery. One panel depicted the various factors controlling blood pressure and bleeding, while others illustrated the historical background of, the indications and contraindications to, and the prerequisites for controlled hypotension. The technique of the procedure was shown together with charts of operation records. Surgical emergencies in the newborn were demonstrated by the University of Manitoba, the recognition and treatment being exhibited in simple but effective style. This exhibit had sternly resisted the temptation to show too much in too small a space.

Paediatrics

That it is not easy to strike a happy medium in this respect was apparent at the stand where the Research Institute of the Hospital for Sick Children, Toronto, displayed the causes, prevention, and treatment of foetal and neonatal morbidity and mortality. Here was such a wealth of material that, although well set out, it would require close study for at least an hour to assimilate all the valuable information offered. Fortunately the visitor was able later to reinforce his memory by reading the summary thoughtfully provided to be taken away. There were two other exhibits in the field of paediatrics. The first, from the Ontario Society for Crippled Children, displayed ingenious special equipment designed to promote activities of normal development in children with cerebral palsy. In the second, from the Royal Victoria Hospital, Montreal, the procedures were depicted which a team of specialists used in the rehabilitation of patients with cleft palates.

Poliomyelitis

Of particularly topical interest were two exhibits concerned with poliomyelitis. The Connaught Medical Research Laboratories, Toronto, demonstrated the various steps in the preparation of poliomyelitis vaccine (Salk). The Research Institute of the Hospital for Sick Children, Toronto, displayed methods of preparation of tissue cultures for the isolation of poliomyelitis and other viruses from pathological specimens.

Also popular with visitors to the exhibition was the demonstration by the Ontario Department of Health of a simple blood-sugar screening test. This is carried out on 0.1 ml. of capillary blood, the result being read within five minutes as below or above 180 mg.%. The test is in use in survey work, with a mobile laboratory, to detect possible diabetics. It strikes the visitor that it might have an application in antenatal work. There was also a well-documented exhibit of the scope of the activities of the Canadian National Public Health Services. The only exhibit from the armed Forces was by the Royal Canadian Air Force, displaying the activities and research work undertaken by its medical branch.

Insurance Medicine

A little-publicized field of medicine is the valuable actuarial work carried out by insurance companies. There were two exhibits in this sphere. One showed the prognostic value of life insurance mortality investigations (New York and Metropolitan Life Insurance Companies); the other charted the cardiovascular–renal mortality in western countries (Metropolitan Life Insurance Company).

More esoteric, perhaps, was the exhibit from the Montreal Neurological Institute of bony abnormalities of the craniovertebral junction of neurological importance. The Shute Institute, London, Ontario, illustrated the effect of alpha tocopherol on peripheral vascular conditions and burns; and Dr. K. A. BAIRD, Lancaster, N.B., displayed his theories and findings on " sensitivity to products of bacteria." Finally the considerable value of slides, transparencies, and similar methods for instructional purposes was fully demonstrated by the Department of Photography, St. Michael's Hospital, Toronto.

MEDICAL AND TECHNICAL EXHIBITION

Just over one hundred exhibitors took space at the display in the Royal York Hotel of pharmaceutical products, medical publications, instruments, equipment, and food products. This was the biggest exhibition of its kind ever held in Canada, and doctors attending the Joint Meeting appreciated the unusual opportunity it gave them to see how the tools of their trade were being improved by the vigorous efforts of the manufacturers.

Since the last Annual Meeting of the B.M.A. in Canada 25 years ago, the drug treatment of many illnesses had

entirely changed. About fifteen of the exhibitors were displaying antibiotic or chemotherapeutic remedies, and the advances in this field are taking place with such rapidity that to remember even the names of the new drugs is becoming disconcertingly difficult. Apart from the antibiotics, there was much to be learned about hypotensive agents, the "tranquillizers," the antihistaminics, the antispasmodics, the anticholinergic drugs, and the new oral diuretics.

Manufacturers of food and milk products put on some very bright displays, and British visitors in particular had many questions to ask about some of the less familiar dietary supplements.

The surgical manufacturers and medical publishers were both well represented. Many ingenious surgical instruments were on display, and among the more unusual items of equipment was an audio-visual heart-sound recorder. Another recorder of a completely different kind was being demonstrated by the Audio-Digest Foundation—a non-profit-making subsidiary of the California Medical Association. This foundation offers to subscribers tape-recorded abstracts of current medical literature and lectures by well-known authorities. These medical "newscasts" are compiled by a professional board of editors, different recordings being made for each main specialty and for general practitioners. The tapes are played over on a machine about the size of a portable gramophone.

Nova et Vetera

A GLIMPSE OF STUDENT LIFE IN ANCIENT ROME

We know little of medical training in classical antiquity, and of pre-Roman methods our ignorance is almost complete. Scientific medicine was brought to Rome by Greeks, and their language long continued there as the normal for medical writing and instruction. Of medical schools at Rome we can say that the body of students was at first the personal following of certain physicians. The relation of these groups to hospitals, and indeed the whole early history of hospitals, is altogether obscure.

Groups of physicians and students at Rome ultimately combined to form societies or colleges, where professional questions were discussed. About the end of the reign of Augustus (died A.D. 14) these societies became organized, and constructed for themselves on the Esquiline Hill a meeting-place, the so-called *Schola medicorum*. Finally, the Emperors built halls or *auditoria* for the teaching of medicine. The professors at first received only the pupils' fees. Not until the time of Vespasian (Emperor A.D. 70–79) were medical teachers given a salary at the public expense. The system was extended by Hadrian (Emperor 117–138) and Alexander Severus (222–235).

Little more can be told of methods of medical instruction in classical times, and even less of the conditions of life of ancient medical students. In this dearth of information an account of a students' frolic in Rome in the days of the Emperor Marcus Aurelius (161–180) does, at least, lift a corner of the curtain. The circumstances inform us, what most of us had guessed, that students then were much like students now.

It must be explained that the incidents turned on the refutation by Galen (130–201), then practising and teaching at Rome, of a prevalent theory that the arteries contain only air, or rather air and *pneuma*, a word often translated "spirit." This theory was associated especially with the name of Erasistratus (*c.* 280 B.C.). The exact nature of pneuma does not here concern us, nor need we discuss Galen's refutation of Erasistratus, who had been dead for about 450 years. But the reader may be reminded that the theory of Erasistratus was not as absurd as it seems, for after death the arteries are almost empty, whereas the veins are usually full of blood. The belief which Galen opposed was that, when an artery was incised during life, the air and pneuma escaped at once, and, as they did so, the vessel instantaneously filled with blood as into a vacuum. About A.D. 170 Galen wrote a book to disprove this view, adducing experimental evidence, which again we need not discuss.

About A.D. 177 Galen issued in Greek his great handbook of dissection and physiological experiment, *On Anatomical Procedures*. It is addressed to students and contains many items of advice and admonition to them. It represents a series of Galen's lectures, taken down in shorthand and revised by him. It thus preserves something near to his actual words, and much of it gives the impression of the rapid give and take of an active and rather irritable teacher dealing with a group of eager students. From it we translate a passage in which Galen records a series of rowdy student demonstrations in his favour and against his opponents.

"Since some, talking impudent nonsense, openly promise to show that the arteries are empty of blood, one giving the lie to the other on actual observations, I too must spend time on this topic.

"One of these pretenders was always promising to exhibit the great artery (=aorta) empty of blood, but never did so. When some ardent youths brought animals to him and challenged him to the test, he declared he would not make it without a fee. They laid down at once a thousand drachmae for him to pocket, should he succeed. In his embarrassment he made many twists and turns, but, under pressure from all present, mustered courage to take a lancet and cut along the left side of the thorax at the point where, he thought, the aorta should become visible. He proved so little practised in dissection that he cut on to the bone!

"Another of the same gang made his cut on to the bone across the intercostal region, and straightaway severed artery and vein. Thus the fellow incurred the ridicule of the youths who had deposited the stakes with the assembled spectators. The youths themselves now carried out what the last had promised, making their incision as they had seen me, without damaging any vessels. Moreover, they quickly applied two ligatures, one immediately beyond the point where the aorta rises from the heart, the other where it reaches the spine. Thus, as the impudent fellow had promised, after the death of the animal it might be seen whether this stretch of the artery between the ligatures were empty of blood. When it was found far from empty, they said that an irruption had taken place into it when the ligatures were applied, as if someone else and not they themselves had undertaken to do the operation, though they were without the necessary experience and were incapable of applying the ligatures faster than others. For they did not even know that an artery and vein follow the lower border of each rib.

"Of the same ilk again was the man who invented the four-edged hatchet, but did not make nor even try it, though he insolently promised to demonstrate with it an artery empty of blood! His dream was something like this. He wanted to get made a four-edged axe, square and coming to a single point whereat a handle was to be attached. Then the animal was to be stretched out on its belly and struck violently on the spine with the axe, so as to cut out a rectangular piece with one blow. With this peculiar outline, he said, the part of the great artery would be included and found empty of blood. This device may be left to the comic writers.

"We may recall yet another effort, that of a pompous septuagenarian who claimed that he would demonstrate an artery empty of blood. The animal must be one that can be readily skinned, as a sheep, ox, or goat. The incision must be made at some point where a large artery lies just beneath the skin. The artery must have the skin removed all round and bared of the surrounding tissues so that it stands free. The cut in the skin must be protected and, after six or seven days, its edges opened and two ligatures put around the artery, as far apart as possible. When the

part between was cut out it would then, he said, be found empty. This old fellow never dared to make his experiment himself, but we did so for him as soon as we heard of it. We tried it on a goat, on kine, and on sheep, as the old man had directed. We then invited him to wake up and see for himself, once and for all, and be convicted of the error of what had appeared to him in a mere dream.

"Moreover, not long since, another fellow gave a totally false account of an experiment described by me in my book *Whether There is Blood in the Arteries.* Those who had observed my experiment were astonished at his temerity and asked him if he had ever performed it himself or merely relied on hearsay. He replied that he had performed it often. So they brought a goat and tried to force him to demonstrate it. He declined, of course, because he did not know how. They then demonstrated to the onlookers that the actual phenomenon was different [from what he said], and thus ended his absurd claims."

CHARLES SINGER.

Preparations and Appliances

PORTABLE OXYGEN INHALER

Dr. RONALD JARMAN, senior anaesthetist, Gordon Hospital for Rectal, Colonic and Gastro-Intestinal Diseases (Westminster Hospital Group), writes: The apparatus here described seeks to provide a self-contained oxygen inhaler which may be carried on the person for the relief of respiratory embarrassment where effort tolerance is low. As with most portable equipment for the inhalation of compressed gases, the main problem is the inherent one of weight/capacity ratio of cylinders. The solution has to be a compromise, and in this case a cylinder containing 22 litres of oxygen and weighing approximately 16 oz. (450 g.) has been selected.

This cylinder is readily available, and is used in conjunction with a combined flow-rate-adjusting valve and seal piercer on the "sparklet" principle. The cylinder is screwed into the threaded orifice of the valve body, after which the control valve is screwed fully in clockwise rotation for the purpose of piercing the seal. The valve may then be opened in anticlockwise rotation to release oxygen from the outlet. This outlet is also threaded and receives the unit to which the facepiece and reservoir bag are attached, together with inspiratory, expiratory, and non-rebreathing valves. The 22 litres of oxygen is contained in the cylinder at a pressure of 2,000 lb. per square inch (140.6 kg. per square cm.). It is customary to employ a regulator for reducing pressure to a more manageable limit, usually about 5 lb. per square inch (0.35 kg. per square cm.), but in order to achieve simplicity and minimum weight this desirable component is omitted. In its place a fixed orifice in the form of a carburettor jet is employed to facilitate flow adjustment at full cylinder pressure. Oxygen is admitted via this jet to the reservoir bag, whence it may be inhaled by the patient's inspiratory effort.

FIG. 2.—Apparatus in use.

A non-return valve in the bag mount inhibits rebreathing. Exhalation takes place through a non-adjustable valve attached to the body of the unit. An adjustable expiratory valve is alternatively available.

A fixed inspiratory valve located on the top of the unit permits the free entry of atmospheric air when the patient's inspiratory requirements exceed the volume available in the reservoir bag.

The duration of the cylinder will depend on the patient's minute-volume and on the proportions of oxygen and atmospheric air inhaled. If the flow of oxygen to the reservoir bag is so adjusted that the bag never completely deflates, then 100% oxygen will be inhaled, and with a minute-volume of, say, 15 litres the endurance would not be more than approximately 1½ minutes. If, on the other hand, the oxygen flow rate is so adjusted that the reservoir bag collapses at about the mid-point of the inspiratory phase, 50% oxygen and 50% atmospheric air—that is, 60% oxygen and 40% nitrogen—would be inhaled, increasing the duration to approximately three minutes. Cylinder replacement may be effected in 20 seconds.

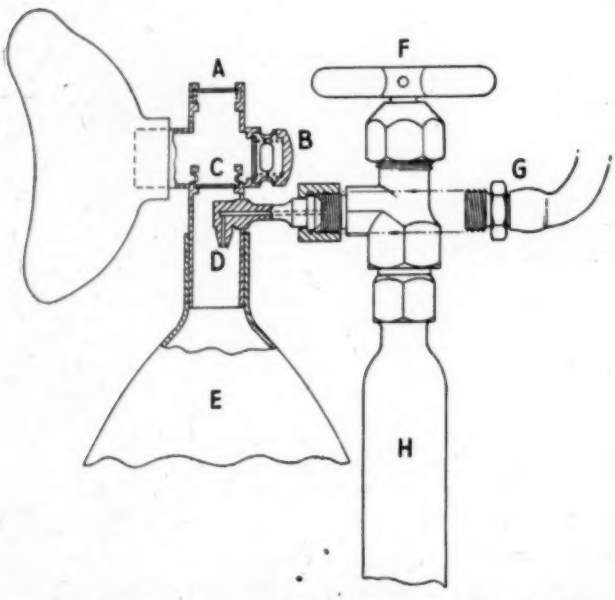


FIG. 1.—A, Inspiratory air valve. B, Expiratory valve. C, Non-rebreathing valve. D, Removable jet for restraining cylinder pressure. E, Reservoir bag. F, Oxygen control valve and cylinder seal piercer unit. G, Rubber tubing adapter. Alternative to "F" for utilizing large cylinders. H, 22-litre screw-neck cylinder.

The inhaler is readily adaptable for use with larger cylinders when extreme portability is not required. The cylinder, with its control valve body, may be detached and a simple rubber-tubing mount substituted. By this means it may be coupled to any of the conventional types of fine adjustment or pressure-reducing regulators commonly used for oxygen therapy. Before doing so, however, it is necessary to remove the carburettor jet; this is a simple procedure. The reservoir bag is first detached, thereby exposing the jet, which may be unscrewed from its mounting by means of a small box spanner with which the apparatus is provided.

The inhaler is of value to people who have bronchial spasms first thing in the morning, or for elderly folk who find it difficult to walk upstairs, and the mental comfort which it can give probably far exceeds its physiological value. In fact, it can be used in practically any case of emergency when administration of oxygen is likely to relieve the patient. To change the cylinder is a matter of moments, and two, three, or four of these can be carried in the doctor's car or stocked in his surgery. The mere fact of having this apparatus at hand gives a great deal of confidence in cases of emergency.

The apparatus has been made by Messrs. A. Charles King with the approval of the British Oxygen Company, Limited.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Tonsillectomy

SIR,—The resurrection of the debate on the relative merits of the guillotine method of tonsillectomy and of dissection seems inevitable since the publication of the paper by Mr. J. C. Campbell and Mr. D. Hunter Smith (*Journal*, June 18, p. 1451). Much wind and fury often seem to be expended in claiming that one method is safer than the other, when, in fact, all unprejudiced surgeons are agreed that in expert hands the two are equally safe; but the emphasis, rightly so, is on the word "expert."

Deaths from tonsillectomy fall into two groups: preventable and, in the light of modern knowledge, unpreventable. The former are due to anaesthesia, haemorrhage, and blue asphyxia—for example, from inhalation of blood or vomit; obstruction by the tongue or a fragment of adenoid; the latter, the so-called cases of white asphyxia, result from sudden cardiac arrest, the cause of which cannot often be established, terms such as status endolymphaticus explaining nothing.

The essential difference between the two operations is that in one, the guillotine, there is a time limit of seconds and the arrest of bleeding is left to nature, and in the other, the dissection, there is no time limit and the bleeding is usually stopped by the surgeon before the patient leaves the operating table. If a child's bleeding is left to nature, which means, at the outside limit of normal clotting time, that arrest may take ten minutes, it is essential that a cough reflex be present to protect the airway, and this reflex must be present as soon as the child has the gag removed from its mouth, when it may be no longer in a position easily and quickly to have the blood removed with a swab or sucker. Thus, this essential safety condition of the guillotine operation surely necessitates light anaesthesia, and the teaching of Campbell and Hunter Smith that "it cannot be too strongly emphasized that, far from being light, the anaesthesia must, on the contrary, be *deep*," would, from the data supplied regarding operation technique in their article, seem highly unsafe—especially in unskilled hands.

They describe how a child has first one tonsil removed and the fossa inspected and palpated, then the other, and finally a leisurely adenoidectomy, after which—and this is the point—the child is only then turned on its side. In the circumstances it is incomprehensible what happens to the blood which rises, in every "quick" guillotine operation we have seen or done, like an all-engulfing tide, not only placing the airway in jeopardy but submerging and completely obscuring the field of operation in a matter of seconds unless steps are taken to control it by suction or pressure, which must surely involve a longer operating time than the 90 seconds which they consider adequate. This objection, however, must in all fairness be construed in relation to their excellent record. Again, the method of anaesthesia described, though undoubtedly safe in expert hands, is not one which can be generally recommended. It is sometimes forgotten that every method of anaesthesia is safe "in expert hands." Obviously so, or the "expert" would discard it. To advocate a method which is a potential danger in the less expert is to perform a disservice to the general safety of anaesthesia. What particular advantage has the gas, oxygen, and ethyl chloride over the safer gas, oxygen, and ether? The question can be answered in one word—none. The induction is not more pleasant for the patient; the depth and duration of anaesthesia are less controllable; the margin of safety is smaller.

One of us (S. R. M.) has had the fortune to be trained by a master in the guillotining *tour de main*, always to have had the helpful services of a senior anaesthetist, most expert in the administration of ethyl chloride, and to have reduced his own "remnant rate" to 5%. Yet the guillotine operation has been abandoned in favour of dissection not because any children have been lost but because premedication was considered generally unsafe before guillotining children in large numbers, while at the same time it was felt on humane grounds that all children should, in fact, be premedicated before operation; because the dissection method is more suitable for instruction for general use both from the point of view of surgery and anaesthesia; and finally because modern attention is becoming focused more on the adenoidectomy and less on the tonsillectomy. Adenoidectomy is far more difficult to do well and the penalties of an incomplete and inexpert removal are greater, since it is possible to cause permanent deafness through damage to the Eustachian tubes or by failing to remove a cause of Eustachian obstruction and middle ear infection.

No matter in which way the relative merits of the two methods are looked at, a leisurely, meticulous adenoidectomy is only possible with a relaxed palate and with no obligation on the part of the surgeon to hurry *at all*. Other considerations, such as avoidance of psychological trauma by careful premedication and unhurried induction, have weight, but are small beside the overriding need to establish adenoidectomy as a precise operation, and to see the "smash and grab" for what it is: an operation of value when faced by the necessity for a rapid turnover, but one with a smaller margin of safety for the inexperienced, undoubtedly easier to do badly than the dissection, and one which, as a consequence, has often brought otolaryngology and anaesthesia into ill repute.—We are, etc.,

STUART R. MAWSON.
F. F. CARTWRIGHT.

London, S.E.5.

Vagotomy with Gastroenterostomy for Duodenal Ulcer

SIR,—Mr. J. H. Johnston in an interesting letter (*Journal*, June 18, p. 1474) refers to the adoption of the Roux-en-Y type of gastrectomy as a method of treating bilious vomiting following gastroenterostomy and vagotomy. The case described had Billroth II and I gastrectomies carried out without relief of symptoms. He also refers to 12 cases where a Roux-en-Y technique accompanied by vagotomy relieved bilious vomiting in cases previously subjected to Billroth techniques.

It is evident that the afferent loop in Billroth II types of gastrectomy is responsible for many post-operative troubles, especially in the high lesser curvature resections carried out at the present time. I do not believe that "valves" of any kind can improve the situation. The almost universal return to Billroth I is a sign of the times. However, at least 40% of cases of duodenal ulceration are unsuitable for Billroth I techniques. The operation has more than its share of post-operative troubles, not the least of which is a high recurrent ulceration rate. Mr. T. J. Butler (personal communication) reports this rate as high as 10% in a large series.

For some years we have adopted a Roux-en-Y type of gastrectomy combined with a Shoemaker or Pauchet resection of the whole lesser curvature and end-to-end anastomosis of stomach and efferent jejunal loop. We anastomose the afferent jejunal loop to the efferent loop by end-to-side technique not more than four inches below the stoma and to the right side. We do *not* do vagotomy. In a series of cases recently reviewed[1] we have been struck by the smooth post-operative course and the rapid rate of weight gain. There has been complete absence of bilious vomiting, nutritional deficiencies, and steatorrhoea. No recurrent peptic ulceration has occurred in our series. As a result of our experience we have now adopted the above technique in all cases of peptic ulceration, and have, so far, been very satisfied with our results.

Schofield and Anderson[2] reported a large series in 1953 in which a Roux-en-Y gastrectomy was employed. Our results have been very similar to theirs, although our technique differs in many respects. The manœuvres employed by us and our experience with the modified Roux-en-Y gastrectomy are now in the course of publication.—I am, etc.,

T. C. J. O'CONNELL.

Dublin.

REFERENCES

[1] *Irish J. med. Sci.*, 1955, in press.
[2] Schofield, J. E., and Anderson, P. St. G., *British Medical Journal*, 1953, 2, 598.

Mistaken Capsules

SIR,—Surely the answer to Dr. R. E. Irvine's problem (*Journal*, June 18, p. 1477) is, as always, "Read the label on the bottle." Official quarters deprecate the colouring of tablets, etc., and with good reason, since the number of such in use is far too great for any simple colour scheme to be devised, and even a comparatively simple scheme is not infallible, as the following incident illustrates.

Recently, during a week-end, a hospital porter changed a 20 cubic-ft. cylinder on a standard anaesthetic trolley. On Monday morning the cylinder label showed that it contained 95% oxygen and 5% carbon dioxide instead of almost pure oxygen. Investigation showed that this error had occurred as a result of three factors. First, the cylinder store has the usual low level of illumination considered adequate in basement corridors; secondly, the cylinder neck was far from clean; and thirdly, the shade of grey paint used in the colour marking of the cylinder was of a very light shade, very much lighter in fact than that shown on the wall charts published by the British Standards Institution.—I am, etc.,

Wrexham. F. B. SINGLETON.

Cost of Treatment

SIR,—In his letter (*Journal*, June 11, p. 1428) Dr. K. M. Tomlinson refers to a publication by this company entitled "From Threadworm to Whooping Cough"—a pamphlet summarizing reports on the use of terramycin (oxytetracycline) in paediatric conditions. Dr. Tomlinson, by referring to the amount of print devoted to this subject in the leaflet, suggests that undue emphasis was given to the treatment of threadworm infection with "terramycin." In actual fact considerably less than one-sixth of this leaflet refers to threadworm infection. Dr. Tomlinson states: "Lest this should escape my notice, detailed instructions were printed about the dosage. . . ." It is largely because a detailed dosage schedule was given in this leaflet that the number of words relating to threadworm comprised as much as one-sixth of the text. Indeed, the dosage instructions accounted for one-third of the section, and were included at length because the dosage of terramycin in threadworm differs from the dosage in other conditions. We feel that it is a duty of pharmaceutical companies to report published dosage schedules in detail for the benefit of physicians.

Dr. Tomlinson goes on to say, "I was exhorted to treat the whole family at the same time." We would hasten to correct any misunderstanding caused by this remark, as no exhortation was given or implied. Reference was made to a number of published reports by independent investigators, all of whom obtained excellent results with terramycin in the treatment of threadworm. Mention was also made of the paper by Wells *et al.*,[1] who state: "Wherever possible, entire families were examined and treated simultaneously." Presumably these workers considered such treatment desirable, and this was reported in our leaflet.

Dr. Tomlinson refers in his letter to correspondence with us regarding the cost of treatment of threadworm infection with terramycin. Dr. Tomlinson did write to us on April 29 requesting details of the cost, and this information was given to him in broad outline. Dr. Tomlinson wrote to us again on May 7 and in his letter to you complains that he received no reply. In our opinion this second letter did not call for a reply.

Dr. Tomlinson's main criticism appears to be that we did not quote the cost of treatment in our leaflet and failed to compare the cost of treatment of the various preparations which are available for the treatment of threadworm. We are under the impression that the medical profession as a whole understand the position of the pharmaceutical industry, which cannot, owing to its export markets, quote prices on literature which is sent all over the world. Different price structures obtain in different countries, and the quotation of home prices on literature leads to endless difficulties. We still feel that most doctors bear with the industry on this point. As to quoting comparative treatment costs—surely this would not only be unwise, in view of individual idiosyncrasies which affect the basis of treatment from patient to patient, but would be improper if carried out by a pharmaceutical company.

We have always felt that we should acquaint doctors with the results of trials carried out on our preparations. We do not feel that, because some may consider a condition "harmless," we should suppress dissemination of appropriate references. We regard it as the physician's prerogative to decide what treatment he will use in a particular patient, and feel that only he can relate the cost to the patient's condition and circumstances. Lastly, in the leaflet referred to by Dr. Tomlinson we merely placed before the profession, without comment, the views of some of their colleagues, and left it for the individual physician to decide whether in certain of his cases the use of oxytetracycline might be worth while.—I am, etc.,

Folkestone. J. A. RODGERS, Director, Pfizer Ltd.

REFERENCE

1 Wells, H. S., *et al.*, *Antibiot. and Chemother.*, 1951, **1**, 299.

Mepacrine in Taeniasis

SIR,—During my last academic year I was greatly impressed by the introduction of mepacrine against taeniasis. It is now four months since I joined the Department of Medicine of the Civil Hospital, Wad Medani. I have administered the drug up to now to about 100 cases of adults and children. It was given on an empty stomach after a light supper. The dose was 8 tablets for adults and relatively less for children. It was in some cases preceded by phenobarbitone as a gastric sedative, ½ to 1 gr. (32 to 65 mg.), according to the state of the patient. The dose of mepacrine was given in portions with ½-hour intervals, or as a single dose if the patient could stand it; it was followed by a saline purge two hours later. The result was 100% success, and the check was that the head was detected in some cases; in others, repeated examination of stools up to three months showed no ova; and in the remainder repeated intestinal evacuants brought out no segments. In all the cases the worms were coloured yellow and no inconvenience was experienced by any patient whatsoever.—I am, etc.,

Wad Medani, Sudan. F. SHAMSEDDIN.

Natural Childbirth

SIR,—Dr. Hazel B. Baker's statement (*Journal*, May 7, p. 1154) that "the majority of women are much too shy of these matters to attend classes or even tolerate private instruction" is so contrary to my experience that I cannot leave it unchallenged. It is my custom with all my maternity cases to ask at a very early stage whether they understand what is happening and will happen, and, if not, would they like to know? With no exception whatsoever, the answer has always been an eager "Yes," often from women who have already had a baby, "but the doctor didn't tell me anything."

During the antenatal period relaxation is one of the earliest routines, and towards the end I explain simply the process of childbirth, with diagrams, so that nothing is unexpected, and the woman is able to recognize what is happening to her and the baby. I am convinced that such preparation is invaluable. The beginning of a first pregnancy is surely not the wrong time, but essentially the right time, for mental and emotional as well as physical preparation for the fundamental fulfilment of motherhood.—I am, etc.,

Nairobi. V. RUTH HUME.

Measles

SIR,—I entirely endorse the views expressed by Dr. John Fry in his letter (*Journal*, June 4, p. 1389) on the uses and abuses of antibiotics. In my own opinion, the lavish and indiscriminate administration of penicillin and other antibiotics, which seems to be the fashion nowadays, is to be greatly deplored, and is likely to be paid for, not only at present by high costs in cash, but also in the future by the advent of unwelcome strains of "penicillin-fast" organisms.

I would like to draw attention to the comment in *Prescribers Notes* (May, 1955, volume 1, No. 11) which quotes from the *Practitioner*[1] as follows: "The convenience of oral penicillin must not be an excuse for its widespread use in the treatment of trivial infections, or for vague prophylactic measures. Indiscriminate dosage with penicillin *by any route* [my italics] is potentially dangerous and must be avoided."—I am, etc.,

Birmingham, 6. C. COLEY GRAYSON.

REFERENCE

[1] Fairbrother, R. W., *Practitioner*, 1955, 174, 28.

SIR,—In view of the recent correspondence on measles, the following case may be of interest.

We were urgently called to see a girl aged 6½ years who had been making an apparently good recovery from measles (sixth day since appearance of rash). The mother said that the child had suddenly complained of headache and tried to vomit, and then found that she was unable to see. Prior to this, she had been lively and very anxious to get up. Examination revealed no abnormality apart from complete blindness. The pupils were central and did not react to light. Half an hour later the child had a fit with clonic movements of the left arm and leg, with deviation of the eyes to the left. After a few minutes the movement ceased, and the child lay in a semi-stuporous state. Further examination now revealed absent patella and ankle jerks on both sides with a positive Babinski response on the left. There was now a definite nystagmus. Some 10 minutes later a further fit took place, and intramuscular phenobarbitone 1 gr. (65 mg.) was now given. Re-examination revealed definite neck rigidity. Some 20 minutes later the child regained consciousness and also her vision, but was unable to move her left arm and leg. Her speech was somewhat slurred, and deviation of the tongue to the left was noted. After a further hour the child was normal in every respect and has had a completely normal convalescence.

The diagnosis would appear to have been one of encephalitis of a somewhat atypical nature. We would welcome the comment of our colleagues on this case.—We are, etc.,

WILFRID F. ADAMS.
Faversham, Kent. J. CANTOR.

SIR,—Congratulations to Dr. Frewen Moor (*Journal*, June 25, p. 1534). He has had the courage to extend to the practice of isolating measles cases the same scepticism that I expressed a few weeks ago (*Journal*, March 19, p. 727) concerning the isolation of chicken-pox cases. I thought of including measles in my remarks, but lacked the courage to face the resultant storm of abuse. Recently I saw over a hundred cases of measles in a local epidemic. All were promptly isolated and kept so until two weeks after the onset of the rash. Nevertheless I cannot think of one case where the younger brothers and sisters of the patient failed to contract the infection unless they had already had it, and I cannot name for certain a single patient attending one of the affected schools who managed to miss it if he or she was susceptible. In other words, it was all a waste of time.

In case Dr. Moor is misunderstood in the same way as I was about chicken-pox, may I point out that neither of us suggests that the affected children should be sent to school while they are still ill enough to be kept home on account of the severity of their symptoms. Furthermore, neither of us approves of the diseases in principle, and no doubt we should both be delighted if somebody could find a way of effectively preventing them.—I am, etc.,

Margate. M. CURWEN.

An Antibiotic-Induced Staphylococcal Enterocolitis

SIR,—I was most interested in Mr. B. J. Fowler's article (*Journal*, May 28, p. 1313) on this subject. A recent case I had fell into a similar category.

A housewife aged 44 was admitted on May 8, 1955, with a tendon sheath infection of the right thumb which had been treated for two days with systemic penicillin. At operation pus was evacuated which looked as though it was of staphylococcal origin. She was given chlortetracycline ("aureomycin") 250 mg. 4-hourly. On May 11 she developed a mild diarrhoea, and so the chlortetracycline was stopped after a total of 4.75 g. At this point the swab from the tendon sheath was returned negative after 48 hours' culture. The following day the diarrhoea had stopped, and she continued well until the evening of May 14, when she had four motions, and she was not quite so well. In the early hours of the next day she suddenly collapsed, became almost pulseless, cyanosed, cold, and sweating, and complained of a mild retro-sternal pain; pulse 120, B.P. not readable. It was felt that she had either a coronary infarction or a pulmonary embolus, and she was given morphine and intravenous fluids into which were added heparin and noradrenaline in sufficient quantity to restore the blood pressure to about 110/60 and keep it at that. However, the E.C.G. and chest *x*-ray were both quite normal and remained so. The serum electrolytes were also within normal limits on May 15. The following day she passed a blood-stained motion, and a swab of this was cultured but grew no *Staphylococcus aureus*. She was given two pints (1.1 l.) of blood and systemic penicillin and remained on intravenous fluids with noradrenaline, but on the morning of May 17 her blood pressure suddenly fell and she died.

At necropsy the right lower lobe was collapsed and showed evidence of a suppurative bronchopneumonia. The pus cultured from this grew *Staphylococcus aureus* which was sensitive to all antibiotics except chlortetracycline. The stomach was injected and there were petechial haemorrhages in the fundus. The small intestine was injected throughout its length, as was the large intestine, and in the descending and pelvic colon there were patches of brown adherent membrane. Unfortunately no swab was taken from the bowel at necropsy. The adrenal glands were normal.

I think that, despite the absence of direct evidence, this must be a case of staphylococcal enterocolitis. The points of interest seem to be: (*a*) It was a non-alimentary condition for which the chlortetracycline was given. Most, though not all, of the cases reported have been given antibiotics for alimentary tract infections or accompanying operative procedures on the alimentary canal. (*b*) The dramatic suddenness of the collapse, which led me to think at first of an intrathoracic catastrophe. Most patients have had diarrhoea or vomiting for a few days beforehand, whereas this patient was in fact constipated until the evening before she collapsed. The mistakes in the management of this case might be: (*a*) The administration of chlortetracycline. I feel that, in view of the length of history and the failure to respond clinically to penicillin, it was justified to give chlortetracycline, though not in the large dosage I did. (*b*) Failure to recognize the condition early enough and to administer erythromycin.

It would also appear from this case, as from some others that have been described, that this syndrome must be taken into the differential diagnosis of those conditions presenting as acute peripheral vasomotor collapse, such as coronary thrombosis, pulmonary embolus, spontaneous pneumothorax, concealed internal haemorrhage, or, indeed, shock from any cause, especially if the patient has been having one of the broad-spectrum antibiotics or a combination of penicillin and streptomycin.—I am, etc.,

Birmingham. P. D. HOOPER.

Diversities of Sex

SIR,—In his article "Diversities of Sex" (*Journal*, May 14, p. 1173) Dr. C. N. Armstrong writes: "There is no doubt that active male homosexuals recognize passive male homosexuals by some means unknown," and goes on to ask if there is some sixth sense which homosexuals possess.

It is interesting in this context to note the description which the French novelist Marcel Proust—himself a homosexual—gives of the meeting of the Baron de Charlus and Jupien in the first volume of *Sodome et Gomorrhe*. The Baron is the active, Jupien the passive, but Jupien is aware of the Baron's attention and interest and reacts, as Proust himself says, like a flower quivering in anticipation of the fertilizing bee. Charlus had, of course, recognized Jupien, and Proust makes the following comment on the charade of their meeting: "One does not arrive spontaneously at that pitch of perfection except when one meets in a foreign country a compatriot with whom an understanding then grows up of itself, both parties speaking the same language, even though they have never seen one another before" (see *Cities of the Plain*, translated by C. K. Scott Moncrieff, 1949, vol. 1, p. 6, Chatto and Windus).

According to Proust, recognition is both instinctive and mutual. A study of similar meetings described in *A la Recherche du Temps Perdu* might perhaps prove to be of some clinical interest.—I am, etc.,

Birmingham. P. M. W. THODY.

Opportunities for Medical Practice

SIR,—The *Journal* of May 14 included an article by Sir Stanley Davidson, "Opportunities for Medical Practice at Home and Abroad" (p. 1171). In all fairness to those interested, I must point out that this doleful picture does not apply in Canada.

A nation's medical needs cannot be ascertained by population statistics only. Surely a more reasonable approach would be to ascertain the medical needs and the demand for medical care of the population in question. From experience in private practice in Canada since the war, it is obvious that, though the population has increased only 25%, the demand for medical care has increased 300 or 400%. This true picture is easily explained: (1) a keen appreciation by the people of what modern medicine has to offer; (2) a refusal to queue for medical care; (3) health insurance coverage of a third of the population; (4) relatively high level of incomes in Canada. Finally, increased specialization in medicine has improved the quality but decreased the output per doctor.

Another feature of post-war medicine in Canada is the phenomenal multiplication of hospitals large and small. Literally hundreds of small rural hospitals and dozens of large city hospitals have been built since the war. Montreal this year is completing 4,000 new hospital beds, including the largest children's hospital in the British Empire. All these hospitals must be staffed. It is the avowed intention of organized medicine in Canada that every practising doctor will have hospital facilities for his use. This is rapidly becoming a reality due to the efforts of the young but robust College of General Practice.

Lest the picture look too bright, let me point out that no doctor, except the dead one, knows security in Canada. The foreign doctor must be willing to conform with Canadian ways and to cater night and day to a very demanding public. Nor is a higher degree, including British degrees, of any great assistance. The Canadian doctor has to prove himself to his public—and a very discerning public it is.

Finally, as a Canadian who has always looked to Great Britain for inspiration, may I say that I do not find it inspiring to read that a move is afoot to reduce the intake to British medical schools. This world is crying out for doctors and expansion should be the word, not contraction. In fact there is room in British medical schools for a "department of indoctrination," its duties to be: (1) breed a healthy suspicion of all human statistics; (2) unmask committee medicine for the dead thing that it is; (3) rediscover the world for Britain and British medicine.

These are some of the thoughts which afflict me as I turn for home after seven interesting and profitable months' postgraduate work in Britain.—I am, etc.,

Wakefield, Canada. J. H. S. GEGGIE.

"Half-minute" Thermometers

SIR,—I have been much interested in, and a little perturbed by, the correspondence on thermometers, from which it would appear that misconceptions on the subject are current. My own experience is that reputable thermometer makers serve us very well and provide us with reliable instruments which it is our obligation to use with intelligence.

Fundamentally, surely, a mercury thermometer gives an indication of the temperature of the mercury in the bulb; the more skilfully the thermometer is made the more accurate this indication is. As the thermometer, and the mercury in it, tend to acquire the temperature of its surroundings, it can be said to give an indication of that temperature too. A little thought should show that several factors can influence the accuracy of this indication, two obvious ones being the construction of the thermometer (form, material, etc.) and the nature of the substance surrounding it. Thus, for example, a cold thermometer with a small, thin-walled bulb, placed in warm water will fairly soon approximate in temperature to that of the water; one with a large thick-walled bulb, placed in cork granules, will take longer to approximate in temperature to its surroundings. (The relationship between "speed" and final accuracy is, of course, another matter.) Other things being equal, a thermometer will probably take rather longer to approximate to the temperature of its surroundings in the axilla than in the mouth or rectum.

An equally—or perhaps even more—important question is how far the temperature of the particular bit of the body with which our thermometer is in contact represents what we consider to be the temperature of the body as a whole. Local cooling, affected by anatomical, functional, and accidental factors, can obviously have a great effect. For example, the mouth temperature may be at least 2° F. (0.75° C.) lower just after ordinary social activities—eating, conversation, etc.—than after the mouth has been kept closed strictly for 10 to 15 minutes. As a student I had satisfied myself by a number of simple experiments that temperature-taking is not just a simple matter of popping a thermometer into the mouth for so many seconds or minutes.—I am, etc.,

London, N.W.3. A. DALBY.

SIR,—With reference to Dr. D. J. Campbell's letter (*Journal*, June 18, p. 1474), and his quotation from Best and Taylor that the normal human oral temperature ranges from 96.6° F. to 100° F. (35.9° to 37.8° C.), some time ago I was struck by what appeared to be an abnormally high number of patients attending the medical extern of the Royal Victoria Hospital whose temperatures were recorded above the usually accepted limit of normal (98.4° F.—36.9° C.).

For interest's sake, therefore, 100 charts were collected at random from the files: of these, 19 had recorded temperatures of 98.6° F. (37° C.) or more, and 12 were 99° F. (37.2° C.) or more. The highest was 99.6° F. (37.55° C.), and the lowest 96° F. (35.6° C.); the average was 97.9° F. (36.6° C.). Of those who had "raised" temperatures, the majority had no disease to account for the pyrexia—a few had chronic bronchitis, one had thyrotoxicosis (99.4° F.—37.4° C.). An interesting thing about the latter was that the patient was admitted the same day to the wards, and throughout her stay of several weeks the temperature remained normal (apart from the usual post-operative pyrexia). The temperatures in extern were taken by the nurse on duty, and presumably the thermometer was left in the mouth for the usual "half-minute." Several thermometers were in use, so that the same one was not used in each case.—I am, etc.,

Belfast. T. D. BROWNE.

Premenstrual Syndrome

SIR,—May I make one or two comments on my friend Dr. G. I. M. Swyer's paper on the treatment of the premenstrual syndrome (*Journal*, June 11, p. 1410)?

In the first place he is quite right in suggesting that mephenesin is a useful treatment. Any treatment which relieves tension in an unspecific way may be helpful, and I have confirmed Dr. Swyer's observation in a still larger series. I haven't talked about it much or written about it at all because (perhaps wrongly) most people do not seem very interested in symptomatic treatment. Now that we have embarked on this course, it might be useful to add that, in milder cases, premenstrual depression often responds to amphetamine and premenstrual headache to aspirin. In the paper to which Dr. Swyer so kindly refers, Dr. Dalton and I[1] were focusing our attention, perhaps too much, on aetiology. We were interested in the fact that in a fair proportion of cases of *all* types, including skin lesions, ethisterone works. This suggests that the action of ethisterone lies at a deeper and more aetiological level than symptomatic remedies picked to relieve individual types of the disorder, sometimes, as Dr. Swyer's paper shows, with equal and perhaps even greater efficacy. I was therefore not surprised to learn that mephenesin scored good results in 61% and ethisterone in 56%, a difference obviously unsignificant in a series of only 23 patients. These are not very different from our result, good in 65%, as opposed to 90% with progesterone. Dr. Swyer's placebo gave good results in 34%. In my simple way, I would gather from this that

progesterone is quite good, ethisterone not so good, and the placebo surprisingly ineffective.

I say surprisingly ineffective because I am convinced that the symptoms of this syndrome are of purely organic origin. As Eric Strauss[2] wrote some time, probably in better chosen words, organic pain is very susceptible to suggestion and psychogenic pain isn't. You can extract a tooth painlessly under hypnosis but you can't cure hysteria that way.

The lesson of Dr. Swyer's paper is that we should not be too highbrow in these matters. Cheap and simple remedies, though contemptibly "symptomatic," often work. Amphetamine, aspirin, and mephenesin are worthy of trial in appropriate cases. When they fail, a few patients will be helped by ethisterone. This is entirely in accordance with my own experience. I would go a little further and suggest that some patients with severe and constant symptoms will need progesterone.—I am, etc.,

London, W.1. RAYMOND GREENE.

REFERENCES

1 Greene, R., and Dalton, K., *British Medical Journal*, 1953, **1**, 1007.
2 Strauss, E. B., ibid., 1949, **2**, 411.

Uterine Inertia

SIR,—Mr. Clifford Kennedy's most helpful paper on uterine inertia (*Journal*, June 25, p. 1522) prompts me to add a note on the value of continuous epidural analgesia in its treatment.

Mr. Kennedy emphasizes that "fear is one of the most important causes." A woman who has entered labour in fear and is now being further demoralized by the pain of hypertonic inertia may be quite unapproachable. Encouragement without practical help only adds to her despair, and speeds the vicious circle. The usual analgesics, even used intensively as Mr. Kennedy recommends, at best give only partial relief. An epidural injection of lignocaine abolishes the pain and transforms the patient's emotional condition. Now one can talk to her, and assure her that her labour, though still likely to be long, will be painless to the end. Since there is no question of general anaesthesia she can take food and drink freely. Labour can safely be allowed to continue longer than it could if she were becoming exhausted. If it has to be terminated by caesarean or other operative means the analgesic zone can be extended as required. Haemorrhage and shock are reduced. The foetus, already under the handicaps described by Mr. Kennedy, is not subjected to further depression by drugs and general anaesthesia.

It takes time and patience to acquire this technique. One has to pass through a period of unreliability and disappointments. But the reward is great.—I am, etc.,

Cambridge H. R. YOUNGMAN.

POINTS FROM LETTERS

Cancer and Thyroid Activity

Dr. A. A. LOESER (London, W.1) writes: Your annotator (*Journal*, May 7, p. 1142) has gone to great pains to disinter the armchair speculations . . . on the possible correlation of thyroid dysfunction and cancer during the last hundred years. . . . The fact cannot be denied that until 1950 (Loeser, A. A., Fifth International Cancer Research Congress, July, 1950, Paris) no clinical therapeutic trials or scientific study had been published as to the place of thyroid in the management of cancer. In looking over his shoulder at the past your anonymous writer has failed to see all of the present. My theme then and more recently (1953–4) was that thyroid is not only a possibly valuable weapon in the armamentarium in the battle against cancer—it is also a prophylactic remedy; and I hope I have proved this not by theoretical speculation but by controlled clinical investigation and scientific studies. My observations have now been confirmed by J. G. Spencer (*Brit. J. Cancer*, 1954, **8**, 393) in his most valuable statistical contribution.

Medical Directory

The Editor of the *Medical Directory* writes: The accuracy of the *Medical Directory* depends on the return of the annual schedule, which has recently been posted to members of the medical profession. Should the schedule have been mislaid I will gladly forward a duplicate upon request. The full name and year of qualification of the doctor should be sent for identification. Communications should be addressed to: The Editor, The *Medical Directory*, 104, Gloucester Place, London, W.1.

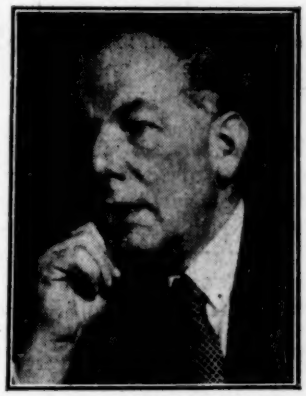
Obituary

STUART LAIDLAW, M.D., Ph.D., B.Sc., B.L.

F.R.F.P.S., D.P.H., D.P.A.

The sudden death on June 24 of Dr. Stuart Laidlaw, medical officer of health for the city of Glasgow, at the early age of 52, has been a severe blow to the public health services of the city and indeed of Scotland.

Stuart Ian Alexander Laidlaw was born in Glasgow on July 7, 1902, but received his early education at the City of London School, returning to Glasgow to read medicine. Before taking his medical degrees, however, he sat the B.Sc. examination, graduating with honours in 1924. Two years later he obtained the degrees of M.B., Ch.B. with commendation and distinction in surgery. He was a Cullen medallist and gained the West of Scotland R.A.M.C. Memorial Prize on his final examination.



[*Picture Post Library*

After holding the usual house appointments, Laidlaw was an assistant physician at Glasgow Royal Mental Hospital, and later had experience of public health work in Fife and of general practice in Glasgow. Then he became senior assistant to the professor of public health at Glasgow University, and in 1929 obtained the D.P.H. In November of the same year he was appointed assistant medical officer to the public health department of the city and in 1930 clinical officer for the Eastern Division, where he investigated the epidemiology of phthisis in young adults, the work culminating in a thesis which earned him the M.D., with commendation, in 1934. In this year he was appointed divisional medical officer to the Northern Division, later moving to the Central Division, and in 1939 he became senior assistant medical officer of health in charge of the tuberculosis services. In this period he added much to the foundation of his knowledge of public health and housing. During the second world war, in addition to his work in the civil defence organization, he carried out investigations into the underlying causes of the increased incidence and mortality from tuberculosis, and was responsible for the development of the mass radiography scheme in the city.

Laidlaw was appointed medical officer of health for the city of Glasgow in 1946, at a time of change just before the inauguration of the National Health Service, and soon displayed his special qualities in masterly adaptation. In succession he tackled the pressing need for more hospital beds and more nurses for tuberculous patients, and for the development of thoracic surgery in tuberculosis, resulting in the fine unit at Mearnskirk. Later he grasped eagerly the chance of developing B.C.G. vaccination, and in 1953, before its general official adoption, he already had a scheme in operation for the protection of schoolchildren.

The impact of the National Health Service on preventive medicine provoked Laidlaw to new lines of thought,

and he explored the need for an industrial health service for the group of smaller factories in Glasgow by pilot experiments in municipal departments and factories. In this field he gave evidence on behalf of the Society of Medical Officers of Health before the Dale Committee on industrial health services, the report of which was published in 1951. The subsequent report, by Laidlaw and J. H. Bell, on occupational health in the Govan ward of Glasgow, published in 1953, reinforced his earlier findings. He also devoted much attention to the aged and chronic sick and handicapped when he carried through the integration of health and welfare services in Glasgow in 1949. Homes for aged and ailing persons were essential to his programme, and he pressed for modern types of hostels to meet what he considered urgent needs. He took an active interest in the work of the Marie Curie Memorial Foundation, and became chairman of the Glasgow committee and warden of Strathclyde House.

Laidlaw was a skilled administrator—he took the London D.P.A. in 1940—and the health services of Glasgow developed and expanded under his care. Atmospheric pollution claimed his attention and his pen, and a smokeless zone in the centre of the city was his aim. The incidence of food-poisoning and the unsatisfactory standard of food hygiene provoked study of the problems associated with food handling, an interest recognized by his appointment last year as president of the Catering Managers' Association of Great Britain. In recognition of his masterly handling of the smallpox outbreak in 1950 the Priory of Scotland of the Venerable Order of St. John conferred on him the honour of officer. He brought fresh thought and consuming interest to all the varied problems connected with human welfare. One of his last tasks was an investigation into Glasgow common lodging-houses and their inhabitants. He spent three years on this inquiry, the results of which were embodied in a thesis gaining for him the Ph.D. of Glasgow University: he was to have graduated on July 9. In 1944 he obtained the Glasgow degree of B.L., and six years later he was elected a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow. He died while visiting a new clinic in one of the housing estates on the outskirts of the city. Laidlaw was a member of the board of management of Glasgow Northern Hospitals, the Advisory Committee on Medical Research, the Scottish Health Services Council, and the Consultative Committee of Medical Officers of Health. His association with the lay press was a very happy one, and he had a flair for commenting succinctly on matters of public interest. Laidlaw was especially fortunate in his married life. His first wife, Marion Gray, was his contemporary at Glasgow University and became a much-loved general practitioner in the city. After her death in 1950 he married Caroline Blenkinsop, an honours graduate of Bristol University, and to his devoted wife and their young son we tender our deepest sympathy. His untimely passing in his prime has left a profound sense of loss among his friends and colleagues. He has left a memory that will endure.—W. A. H.

C. M. FINNY, O.B.E., M.B., F.R.C.S., D.P.H.

Major-General C. M. Finny, formerly deputy director of medical services, Northern Command, died suddenly at his home at Camberley, Surrey, on June 20. He was 68 years of age.

Charles Morgan Finny was born in Dublin on July 9, 1886, the son of Dr. J. Magee Finny, and was educated at Shrewsbury and Trinity College, Dublin, graduating M.B., B.Ch. in 1910 and taking the Dublin D.P.H. two years later. He obtained the diploma of F.R.C.S. in 1921. He entered the R.A.M.C. in 1911, serving in India, South Persia, and Malta, as well as throughout the first world war. Appointed O.B.E. in 1927, he became lieutenant-colonel in 1934, and six years later, soon after the outbreak of the second world war, he was appointed assistant director of medical services of the 3rd Division. From 1940, by which time he had attained the rank of temporary brigadier, to 1942 he was an honorary surgeon to the King, and in 1941 he became deputy director of medical services, Northern Command, having previously served in the similar appointment with the Third Corps. He retired towards the end of 1941, but in the following year was recalled for duty, with the rank of colonel, for the remainder of the second world war. He finally retired in 1946 with the rank of major-general. He married Miss Doris Manners Smith, daughter of Lieutenant-Colonel J. Manners Smith of the Indian Army, in 1928, and had two daughters.

Dr. E. HARVIE COX, the oldest medical practitioner in Rochdale, Lancashire, died at his home there on June 3 at the age of 77. Edward Harvie Cox was born at Manchester on April 5, 1878, and was educated at Manchester Grammar School and at King William's College, Isle of Man. He then entered Manchester University as a medical student and graduated M.B., Ch.B. in 1903. After holding resident posts, including that of assistant surgical officer, at Manchester Royal Infirmary, he began practice at Rochdale in 1907. During the first world war he served with the R.A.M.C., becoming a lieutenant-colonel, and was awarded the D.S.O. for his work in France and the Dardanelles. He retired from the position of hon. surgeon to the Rochdale Infirmary in 1942, having held the appointment since 1911. Until his retirement ten weeks before his death he held the post of Treasury medical officer for Rochdale. From 1927 to 1930 he was chairman of the Rochdale Division of the British Medical Association. He is survived by his widow and a married daughter.

Dr. J. F. KNOX writes: It was in keeping with his character that Dr. E. Harvie Cox should have continued actively with his professional work as long as he was able to do so. He was a man of high standards and firm principles. These were rather unbending at times, but he held the respect of his colleagues and the affection of his patients by his sincerity and his consistency. In recent years his erect and soldierly figure became stooped from a chronic rheumatic condition, but he made no complaint. A fracture of the neck of the femur in 1952 from a fall in icy conditions kept him off his work for almost a year, but the union of the fracture in a corrected position enabled him to get about even better than before. The great efforts required to take on professional work again would have deterred many, but Dr. Cox was the type of man who was inspired by difficulties and he never doubted his own capacity to succeed. He was a fine example of the family practitioner who accepted the challenge of the times he lived in and strove, with success, to maintain the highest ideals of his profession. His colleagues, who mourn his passing, are grateful for his example.

Dr. JANET S. DARLING died at Kingston, Ontario, on June 8 at the early age of 29. Janet Stella Darling was born on May 22, 1926, the younger daughter of the late Dr. William Darling, who died in 1931, and was educated at George Watson's Ladies' College and Edinburgh University, where she graduated M.B., Ch.B. in 1949. Three years later, after

having gained experience in varied hospital appointments at Edinburgh, Bradford, Halifax, and Dumfries, she joined her sister and brother-in-law, Drs. Margaret H. and Allan McDiarmid, and their colleague in general practice at Sighthill, Edinburgh. In 1954, in order to further her knowledge in children's diseases, Dr. Darling went to Canada—her mother's birthplace—to work in the paediatric department of Kingston General Hospital, Ontario. She was to have returned to Edinburgh to resume work at Sighthill in September, but at the beginning of June contracted the acute and fulminating illness from which, after only a few days, she died. As well as her mother and sister, there are left two brothers, Dr. W. J. E. Darling, of Salisbury, Southern Rhodesia, and Dr. A. H. Darling, of Bourton-on-the-Water, Gloucestershire.

Edinburgh colleagues write: Apart from her professional skill and efficiency, which were considerable, Janet Darling will always be remembered for her cheerful, lovable personality, essentially interested as she was in others, and sensitive to their needs. The high esteem and affection in which she was held by friends, colleagues, and patients alike are manifest not only in the numerous letters received by her family but in the unremitting care with which she was surrounded during her last illness, nurses from her own (paediatric) unit giving up their off-duty time to look after her, so that she should never be without a "special" nurse. It was the privilege of one of us to have Janet Darling as house-surgeon soon after she graduated. Even in those early days she was a clever doctor, but that, of course, was not the secret of the love she inspired in those who met her and worked with her. One remembers chiefly her unfailing good humour and willingness to help, however long and difficult the day's work, and the atmosphere of friendliness which she radiated. All her patients, from the highest to the lowest, were immediately at their ease and confident when she was with them. It is hard to believe that we have lost her so soon.

Dr. JESSIE J. STOOKE died at her home at Sutton Coldfield, Warwickshire, on June 13 at the age of 80. Jessie Jane Graham was born at Dunfermline on May 4, 1875, and received her medical training at Edinburgh, taking the Scottish triple qualification in 1900. She then went to China, where she was married in Shanghai cathedral to Dr. George Frederick Stooke, a contemporary of hers at Edinburgh and a medical missionary working with the Church of Scotland Mission at I'Chang, Central China. After the death of her husband in a cholera epidemic in 1908, Dr. Stooke for a time superintended both the hospital and the consulate at I'Chang, work for which she received a letter of thanks from the then Foreign Secretary. She came back to Dunfermline in 1909, leaving for a short period to act as resident medical officer at the Lurgan workhouse and hospital in Co. Armagh, and returning in 1912 to become a school medical officer under the Carnegie Trust. In 1911 she obtained the D.P.H. of the Scottish Royal Colleges, and four years later went to live at Gravelly Hill, Birmingham, on becoming a whole-time school medical officer there. She held this appointment until 1940, when she retired, but continued in a part-time capacity for the remainder of the second world war. Dr. Stooke was a past president of the Birmingham Association of the Medical Women's Federation. She is survived by one son, Dr. J. G. Stooke, and two daughters.

Dr. ISAAC NEWTON, a direct descendant of Sir Isaac Newton, died at Lichfield, Staffordshire, on June 24 at the age of 87. Isaac Newton was born on August 17, 1867, and was educated at Epsom College, receiving his clinical training at Charing Cross Hospital. He qualified M.R.C.S., L.R.C.P. in 1892, and almost immediately settled in practice at Tonbridge, Kent, at first in association with Drs. John Gorham and Eyre Ievers. In 1895 he became medical officer to Tonbridge School, and held the appointment until 1929, when he retired and went to live at Budleigh Salterton, in Devonshire. From 1938 onwards he lived successively at Burgess Hill, Sussex; Duntisbourne Abbots, near Cirencester; Cranbrook, Kent; and Bridgnorth, Shropshire; spending the last few years of his life with one of his sons, Mr. Patrick Newton, senior master at St. Chad's School, Lichfield. It was while at Lichfield last year that Dr. and Mrs. Newton celebrated their diamond wedding anniversary.

Medico-Legal

INJURED MOTOR-CYCLIST

TRUMPERY BUT DIFFICULT CASE

Mr. Justice Pilcher, giving judgment in a civil action at Bristol Assizes on July 1, suggested that in certain cases it might be advisable for hospital management committees to make a small payment to plaintiffs without any admission as to liability rather than have experienced doctors and surgeons "dragged through the courts." The action was one in which 35-year-old Frederick Henry Kilburn, of London Colney, Herts, was awarded £20 damages with costs against the Swindon and District Hospital Management Committee for pain and suffering which he alleged was due to negligence. The previous day the judge had given a warning against starting actions against individual doctors for negligence or against hospital management committees in cases where damages were likely to be small.

Kilburn said that after he had fallen from his motor scooter he was discharged from Savernake Hospital, near Marlborough, without receiving proper treatment for two fractures in his left knee and a fracture of the right wrist. He said that after sticking plaster had been put on his knees he was given a cup of tea and sent on his way. Later he was admitted to the Royal Berkshire Hospital, Reading, where he was *x*-rayed, and subsequently he was transferred to an annexe of the Royal Cornwall Infirmary.

Mr. R. O. Wheeler, then acting casualty officer at Savernake Hospital, said that after examining Kilburn he concluded that the man had been shaken up but could go on his way after a cup of tea.

The judge said the only criticism that could be levelled at Mr. Wheeler was that at Reading a doctor saw this man about two and a half hours later and had no hesitation in recommending an *x*-ray, and then the whole thing was diagnosed. Mr. Wheeler's examination was not a proper one, and could not be expected to discover what was wrong. Although this was a trumpery case, it was a difficult one. In these days, he continued, when through paying a weekly sum everybody had a right to hospital treatment, one should not start actions against individual doctors for negligence, or against hospital management committees in cases where the damages, if they succeeded, were minimal. He did not think Kilburn was in the least irritated by what happened until he found what a fuss they made of him at Reading.

The judge said that damages would necessarily be small, because the treatment which Mr. Kilburn said he did not receive at Savernake Hospital he did in fact receive three or four hours later at a Reading hospital. He was detained in that hospital for some weeks, and in a hospital in Cornwall for a further four or five weeks, but that was because he developed plaster sores.

"In this type of case one feels every sympathy with an experienced medical man who is attacked professionally, as Mr. Wheeler is attacked in this case. Here is this man, Mr. Kilburn, in a very dirty state, wearing half a dozen coats and jumpers and not having shaved for a week—altogether not a very pleasant spectacle. He was a mountain of a man, 22 stone (140 kg.), and, although I was not suggesting that all this made any difference to the doctor or the nurse, he was obviously going to be a very awkward customer in any hospital. I don't think I should be doing my duty unless I came to the conclusion that, perhaps rather naturally, the doctor did not do more to the plaintiff's leg than the plaintiff himself says and the nurse confirms. The only conclusion at which I can arrive, with great reluctance,

is that on this particular afternoon Mr. Wheeler did fail to examine the plaintiff's left leg in the fashion which is agreed to be the proper fashion, and the fashion which would almost necessarily put him on his guard and lead him to suspect some further injury.

"I appreciate the great services the medical profession render to the community and the difficulties they encounter under the present system. One does not need to sit in these courts for long to appreciate the number of claims which are made against hospital management committees, some in circumstances which are completely unjustified, and sometimes in cases where the damage must be quite trivial. And this is one of those cases.

"It is no part of my duties," he said, "to give any advice to hospital management committeees, but where there may be a doubt as to whether a professional man in any particular instance has fallen short of the high standard one expects, I am inclined to wonder whether there may not be occasions in which rather than take the risk of an experienced doctor or surgeon being, if I may use the phrase, dragged through the courts, a small payment to the plaintiff might be advisable without any admission as to liability."

Before the hearing of the action the Medical Defence Union, of which Mr. Wheeler is a member, accepted full liability for any damages that might be awarded against the hospital management committee.

DOVER BATTLE OF BRITAIN MEMORIAL HOSPITAL FUND

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Even before 1939 the building of the Royal Victoria Hospital, Dover, had become inadequate to fulfil its function as a general hospital. During the war it became very dilapidated and suffered damage from cross-Channel shelling, and in 1944 leading citizens of the town decided to collect a fund to commemorate the Battle of Britain by building a new hospital. They aimed to collect £250,000, and in April, 1945, circulated a pamphlet headed "Dover's Battle of Britain Memorial Hospital" in which the object of the fund was set out: "Our appeal for aid has a twofold objective. The first is for funds to build a new essential hospital and maternity home, and the second is that embodied in it a working memorial feature shall stand for all time in honour of the heroes of the Battle of Britain."

By April, 1946, £25,000 had been collected from Britain, the Commonwealth, and the United States by way of individual donations and from anonymous donors, collecting boxes, proceeds of dances and whist drives, special appeals and collections, and other such activities. But when the National Health Service Bill was published and later became law on November 5, 1946, subscriptions fell off. By July 5, 1948, when the Act took effect, £33,500 had been collected, and a total of £34,000 was ultimately reached.

A site suitable for a new hospital was bought, but the trustees, with £17,500 left with which to build and in view of the fall in subscriptions, came to the conclusion that the scheme had become impracticable and decided to discontinue the appeal. The question therefore arose what was to be done with the money, and whether the named and ascertainable donors were entitled to get back the amount of their donations, since the object of the gift had become impracticable.

The problem was decided on a summons brought by the trustees before Mr. Justice Upjohn in the Chancery Division on June 28, 1955.[1] He came to the conclusion that the individual donations must be presumed to have been made with a general charitable intention, especially having regard to the admixture of the donations from named donors with funds from the various anonymous sources, and that therefore he must deny any right to a return of their money to contributors. Accordingly he ordered a scheme to be prepared in Chambers for the application of the money to another charitable purpose as close as possible to the original object of the fund.

[1] *The Times*, June 29, 1955.

Medical Notes in Parliament

New Hospital Building Programme

Thirty-five major projects in the first programme of new hospital building since the war have been named by the MINISTER OF HEALTH. This programme, which was announced by Mr. Iain Macleod last February, is to be spread over the two years 1956–7 and 1957–8. It includes nine new general hospitals and the beginning of three new teaching hospitals. Some of the projects the Minister mentioned in February—a new teaching hospital at Cardiff, mental hospitals in Lancashire and Yorkshire, and general hospitals at Slough and Boston—are not included in this list because they are not likely to be ready to start before 1958–9. The total value of the schemes selected exceeds the £17,500,000 which has been fixed as the ceiling, and the Minister states that those which are ready first are likely to be started first; any which fail to start in the next two years are likely to have first claim on the resources available in 1958–9.

The complete list, announced by the Minister in the form of a written reply to a question by Mr. J. K. VAUGHAN-MORGAN (Reigate, C.), is as follows:

Regional Hospital Board	*Project*	*Provisionally scheduled to start*
Newcastle	New hospital for West Cumberland	1956–7
Newcastle	Prudhoe and Monkton Mental Deficiency Hospital Development Scheme—Phase I	1956–7
	Phase II	1957–8
Newcastle	Middlesbrough General Hospital Accident and Orthopaedic Dept.	1956–7
Leeds	New Hospital at Huddersfield Phase I	1957–8
Sheffield	Scunthorpe and District War Memorial Hospital Development Scheme	1956–7
Sheffield	Aston Hall Hospital Extensions	1957–8
Sheffield	Doncaster Royal Infirmary Development Scheme	1957–8
East Anglian	St. Luke's Hospital, Lowestoft, Reconditioning Scheme	1956–7
East Anglian	Peterborough and District Memorial Hospital—Extensions	1957–8
North-east Metropolitan	North Middlesex Hospital—New Out-patient Department	1956–7
North-east Metropolitan	South Ockendon Hospital—Extensions	1956–7
North-east Metropolitan	New Hospital for Harlow Phase I	1957–8
South-west Metropolitan	St. James' Hospital, Balham — Development Scheme Phase II	1956–7
South-west Metropolitan	New hospital for Crawley Phase I	1956–7
Oxford	New hospital for Swindon Phase I	1956–7
South-western	Southmead General and Stapleton Hospitals—Geriatric accommodation	1956–7
South-western	Digby Hospital—Additional accommodation for mental patients	1956–7
South-western	New hospital at Truro	1957–8
Welsh	West Wales Hospital, Glangwili — Development Scheme Phase I	1956–7
Welsh	Caernarvon and Anglesey Hospital, Bangor—Development scheme	1956–7

Regional Hospital Board	*Project*	*Provisionally scheduled to start*
Welsh	New hospital at Swansea Phase I	1957–8
Welsh	Llanfrechfa Grange Mental Deficiency Hospital—Extensions	1957–8
Birmingham	New mental hospital at Seisdon Phase I	1957–8
Birmingham	New hospital at Coventry	1957–8
Manchester	Cranage Hall Hospital—Additional accommodation for mental defectives	1956–7
Manchester	New hospital at Wythenshawe Phase I	1957–8
Liverpool	Newchurch Mental Deficiency Hospital—Extensions	1956–7
Boards of Governors		
United Newcastle Hospitals	Royal Victoria Infirmary—New out-patient department	1957–8
United Leeds Hospitals ..	General Infirmary—Extension to out-patient department	1956–7
United Sheffield Hospitals ..	New teaching hospital, Glossop Road—Phase I (Out-patient Department)	1956–7
United Cambridge Hospitals	Addenbrooke's Hospital—Development Scheme first phase	1957–8
United Manchester Hospitals	Royal Infirmary — Reconstruction Scheme	1956–7
University College Hospital	New dental hospital—Mortimer Market, W.1	1956–7
Charing Cross Hospital ..	New hospital at Northwick Park	1957–8
Guy's Hospital	Guy's Hospital surgical ward block	1957–8

The Minister also listed the following ten major projects already in progress or expected to start in the current financial year:

Newcastle	Newcastle General Hospital—Pathological Institute and Regional Blood Transfusion Centre
Sheffield	Balderton Mental Deficiency Hospital—Development Scheme—Phase I
North-west Metropolitan ..	New Hospital at Welwyn—First Phase
South-east Metropolitan ..	Lewisham Hospital—New out-patient department
South-west Metropolitan ..	Horton Hospital Estate—Centralization of boilers
Birmingham	Coventry and Warwickshire Hospital—Development Scheme—Phase III
Liverpool	New mental deficiency hospital—Greaves Hall—Phase I
United Bristol Hospital ..	Royal Infirmary—Joint University Heating Scheme
United Oxford Hospitals ..	Radcliffe Infirmary—Development Scheme
St. Thomas's Hospital ..	St. Thomas's Hospital—Reconstruction

Undermanned Areas

Mr. VAUGHAN-MORGAN asked the Minister of Health what percentage of the population in England and Wales were living in under-doctored areas at October, 1951, April, 1953, and at the latest available date. Mr. MACLEOD stated on June 30 that information was not available in exactly the form asked for, but the percentages of the population on doctors' lists, and living in areas which had been regarded by the Medical Practices Committee as those where doctors should be encouraged to practise, had over the years been broadly as follows: July, 1952: 50%; July, 1953: 37%; July, 1954 (the latest date for which figures are available): 27%.

Cost of Prescriptions

The MINISTER OF HEALTH informed Mr. VAUGHAN-MORGAN on June 30 that the average cost per prescription prescribed through the Health Service in England and Wales during September, 1954, was 51.00d. The figures for the previous months in 1954 were: January, 48.59d.; February, 48.59d.; March, 49.45d.; April, 50.38d.; May, 50.68d.; June, 51.33d.; July, 51.49d.; August, 51.73d. The figures did not cover medicines supplied by doctors who had undertaken to supply their patients direct, nor medicines dispensed at hospitals.

Medical Aspects of Nuclear Radiation

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Prime Minister on June 28 when the White Paper on the possible harmful effects of nuclear explosions would be issued; and whether he would instruct the British delegate to propose in the United Nations that a commission should be established to study and assess the potential dangers in atomic and thermonuclear bomb tests. Sir ANTHONY EDEN said that he was informed that the Medical Research Council were giving the highest priority to the preparation of a report on the medical aspects of nuclear radiation, but they could not yet say when it was likely to be ready. The United States representative to the United Nations made a proposal on June 21 that the United Nations should assemble and collate scientific information from all over the world on the effects of radiation on human health and safety. Her Majesty's Government had learned with interest of this proposal. It would be given careful study, and the Government would be ready to take their full part in discussing it at the first convenient opportunity.

Health Service Reciprocity

Lieut.-Cmdr. L. MAYDON (Wells, C.) asked the Minister of Health with what countries there were reciprocal agreements entitling British subjects to similar benefits to those enjoyed by foreigners who used our Health Scheme. Mr. MACLEOD, on June 29, gave him the following information about foreign countries:

Multilateral Agreements.—A reciprocal agreement is in force between the United Kingdom, France, Belgium, the Netherlands, and Luxembourg for giving medical treatment to indigent persons. A Convention for extending this arrangement to all members of the Council of Europe was signed in December, 1953, and is in force between those countries which have ratified it (the United Kingdom, the Irish Republic, the Netherlands, Norway, Denmark, and the Saar).

Bilateral Agreements.—Agreements are in force whereby British subjects employed in France, Italy, the Netherlands, and Luxembourg who participate in the social insurance schemes of those countries can have their United Kingdom insurance taken into account in reckoning their entitlement, and that of their dependants, to medical benefit. Agreements with Austria, Belgium, the German Federal Republic, and Sweden are being negotiated.

Effects of Fluorine on Stock

Mr. ELLIS SMITH (Stoke-on-Trent, South, Lab.) on June 28 asked the Minister of Agriculture, Fisheries, and Food what research had been undertaken and what had been the results concerning the fluorine pollution of the air in Fenton, Longton, Stoke-on-Trent, and other parts of the country; and what research had been undertaken at the request of the National Farmers' Union. Mr. HEATHCOAT AMORY replied that his department was studying fluorosis in livestock at Fenton Manor Farm, Stoke-on-Trent. The work included experimental treatment to alleviate its effects on cattle: no firm conclusions on this could be expected for some time. Pigs and poultry were being reared there, apparently without ill-effect. Surveys to assess the extent of danger to stock in some other industrial areas were nearing completion. These investigations represented the extension of work on fluorosis which the N.F.U. desired to see.

Poliomyelitis Vaccine

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister of Health on July 4, in view of the fact that an antipoliomyelitis vaccine could be prepared with the use of eggs to be administered by mouth, if he would cancel his orders for the Salk vaccine prepared from monkey tissue. Mr. MACLEOD said he was advised that the development of an egg vaccine against poliomyelitis was still in the experimental stage; in the circumstances it would be unwise to reject other available vaccines, subject to all proper safety tests. He added that it might well be true that in the end cultivation in an egg would be the answer, but it would be unwise to neglect all the other advances that had been made until they were sure of that.

Mr. PETER FREEMAN (Newport, Lab.) asked the Minister whether he would give the details of the method employed to prove that the Salk vaccine was not injurious; and how many children were being given this treatment. Mr. MACLEOD stated that the methods of testing to be employed had not yet been finally settled. No children were receiving this treatment under arrangements made by this country.

Doctors' Surgeries Inspection

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked the Minister of Health whether he would make a statement regarding the progress made in the inspection of doctors' surgeries. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, said that these inspections were being carried out under arrangements made by the British Medical Association; it was understood that they were progressing well. The Association could not yet say exactly when they would be completed, but would let the Minister have a report as soon as they could.

Road Traffic Bill

Mr. HUGH MOLSON, the Joint Parliamentary Secretary to the Ministry of Transport and Civil Aviation, said on July 4 during the second reading of the Road Traffic Bill that despite the increase in the number of vehicles on the road, which was double that before the war, the number of children killed last year was 616 compared with 1,069 in 1938. The number of casualties per 1,000 vehicles had fallen from 99 in 1934 to 41 in 1954. Speaking of the law relating to being drunk in charge, Mr. Molson said that the matter had aroused much public discussion. Recent decisions by courts had stated that the law was unreasonable. In many cases an unfit driver was encouraged to drive home. When the Bill was in Committee the Government hoped to introduce a distinction between driving while under the influence of drink and being drunk in charge of a car. Mr. CHUTER EDE (South Shields, Lab.) regretted that the medical profession, when dealing with a middle-class driver, did not understand that a person could be drunk. He recalled a doctor who went into the witness box and said that "drunk" was a colloquial term he did not understand, and that the jury should decide whether someone was drunk or not. Mr. Ede did not think that merely to smell of drink was evidence of drunkenness, nor did he believe in blood tests, because capacity for drink varied. He hoped that the medical profession would face up to their heavy responsibilities and assist rather than confuse jurors. Mr. CHARLES PANNELL (Leeds, West, Lab.) hoped that a second or third conviction for being drunk in charge would result in the offender being taken off the road for life. He agreed the law should recognize the difference between the drunk driver and the man who was drunk in charge. Those people who deliberately threw the key into the back of the car and slept off the effects had the virtue of knowing that they might be a danger if they drove.

Disabled War Pensioners.—In 1955 there were 634,100 disabled war pensioners, of whom 10,670 were receiving constant attendance allowances, and 16,470 were receiving allowance for lowered standard of occupation. The corresponding figures for 1954 were 655,600, 10,840, and 17,410.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 18** (No. 24) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire	Eire	Eng. & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	10	2	4	0		20	1	4	0	1
Dysentery	859	61	388	17		896	90	228	5	4
Encephalitis, acute	2	0		0		2	0	0	0	
Enteric fever:										
Typhoid	6	0	0	0		3	0	0	1	7
Paratyphoid	11	0	0	0		11	1	13	0	
Food-poisoning	263	23		0		266	22		0	
Infective enteritis or diarrhoea under 2 years				11	18				17	19
Measles*	21,832	496	205	150	341	3,106	93	149	226	345
Meningococcal infection	16	0	8	4		22	1	19	4	2
Ophthalmia neonatorum	46	1	8	0		39	1	13	0	
Pneumonia†	393	15	177	5		309	23	124	3	4
Poliomyelitis, acute:										
Paralytic	21	4	6	2	1	20	1	13	3	
Non-paralytic	8	2				12	1			
Puerperal fever§	239	42	7	4		239	35	8	1	
Scarlet fever	587	49	78	43	23	651	42	107	24	25
Tuberculosis:										
Respiratory	774	66	141	30		904	121	156	42	
Non-respiratory	120	13	19	6		134	12	24	8	
Whooping-cough	1,666	51	90	88	58	1,970	86	246	29	49

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	1	0	1	0		0	0		0	
Encephalitis, acute		0			0		1			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	0	0	1	7	0	1	0	0
Influenza	6	0	0	0	0	2	0	1	1	1
Measles		0	2	0	1		0	0	0	1
Meningococcal infection		0	0				0	1		
Pneumonia	187	20	16	6	13	154	20	12	5	3
Poliomyelitis, acute	2	0			0	0	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	61	8	10	0	1	84	12	9	1	4
Non-respiratory		0	2	0	0		2	1	0	2
Whooping-cough	1	0	0	0	0	3	0	0	0	0
Deaths 0–1 year	216	28	24	2	26	222	31	26	5	15
Deaths (excluding stillbirths)	4,819	664	494	108	174	4,695	666	525	98	149
LIVE BIRTHS	7,973	1245	871	193	465	8,436	1197	923	242	419
STILLBIRTHS	168	21	19			192	19	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Quarterly Returns for Scotland

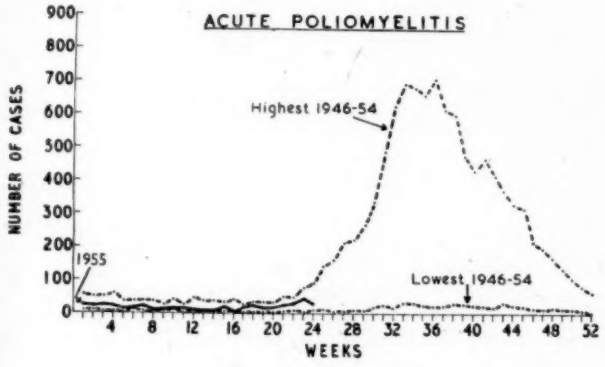
The birth rate during the March quarter of 1955 was 18.3 per 1,000 of the population, being 0.3 below the rate for the first quarter of 1954 and 0.1 below the average March quarters for the five years 1950–4. The infant mortality rate was 36 per 1,000 registered live births; this was 2 below the rate for the corresponding quarter of 1954 and 4 below the five-years average. The general death rate was 15.1 per 1,000 of the population and was 0.8 above the corresponding rate for 1954 and 0.1 above the five-years average. The death rate for all forms of tuberculosis was 25 per 100,000, that from respiratory being 22. Both these rates were 6 below the rate for the first quarter of 1954 and they were 21 and 19, respectively, below the five-years average. 179 deaths were attributed to the principal epidemic diseases, 88 more than in the first quarter of 1954. These deaths included 153 from influenza, 12 from measles, 7 from meningococcal infections, and 5 from whooping-cough. No deaths were recorded from diphtheria or typhoid fever. Deaths from violence numbered 746, and of these 112 were attributed to road transport accidents. Deaths from all forms of violence were 27 more and road transport accident deaths were 21 fewer than in the first quarter of 1954. Accidental falls of persons aged 65 and over accounted for 162 of the deaths from violence.

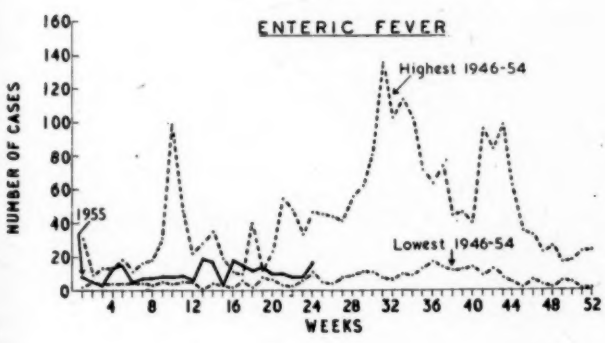
Week Ending June 25

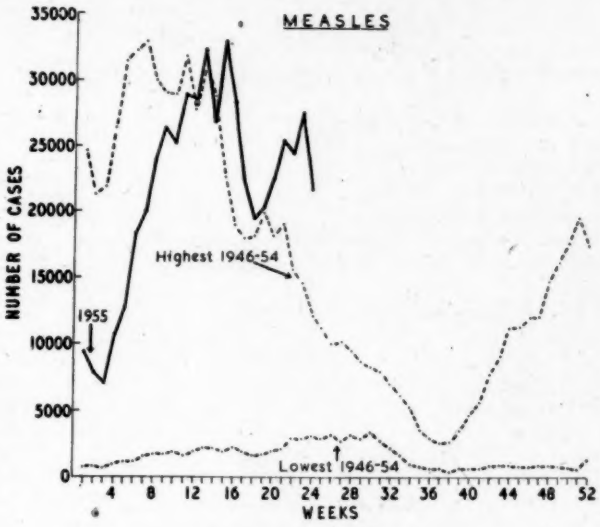
The notifications of infectious diseases during the week included: scarlet fever 541, whooping-cough 1,823, diphtheria 18, measles 20,515, acute pneumonia 358, acute poliomyelitis 54, dysentery 862, paratyphoid fever 23, and typhoid fever 1.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Infectious Diseases

The largest fluctuations in the notifications of infectious diseases in England and Wales during the week ending June 18 were decreases of 5,761 for measles, from 27,593 to 21,832, 115 for whooping-cough, from 1,781 to 1,666, and 96 for acute pneumonia, from 489 to 393, and an increase of 141 for scarlet fever, from 446 to 587.

The largest falls in the incidence of measles were 599 in Yorkshire West Riding, from 2,009 to 1,410, 525 in Middlesex, from 1,630 to 1,105, 484 in Kent, from 1,634 to 1,150, 436 in London, from 932 to 496, 436 in Leicestershire, from 1,386 to 950, 358 in Southampton county, from 1,632 to 1,274. The largest rises in the number of notifications of scarlet fever were 30 in Lancashire, from 64 to 94, and 25 in London, from 24 to 49. The only large fall in whooping-cough was 31 in London, from 82 to 51. 10 cases of diphtheria were notified, 5 fewer than in the preceding week. These cases were notified in four areas, Liverpool C.B. 3; Hertfordshire, Elstree R.D. 3; London, Islington 2; Leeds C.B. 2.

8 of the 11 cases of paratyphoid fever were notified in Sussex (Brighton C.B. 5, Horsham R.D. 2, Horsham U.D. 1).

29 cases of acute poliomyelitis were notified, and these were 14 fewer for paralytic and 1 fewer for non-paralytic than in the preceding week. The largest returns were Yorkshire West Riding 9 (Barnsley C.B. 3, Dodworth U.D. 2), London 6 (Stepney 2).

The notifications of dysentery numbered 859 and were 4 more than in the preceding week. The chief centres of dysentery were Lancashire 230 (Liverpool C.B. 70, Blackpool C.B. 32, Middleton M.B. 18, Blackburn C.B. 16, Salford C.B. 16, Manchester C.B. 13, Stretford M.B. 13), Surrey 80 (Croydon C.B. 56, Banstead U.D. 14), Durham 79 (Stanley U.D. 21, Gateshead C.B. 20, South Shields C.B. 11), Yorkshire West Riding 76 (Huddersfield C.B. 39, Leeds C.B. 17), London 61 (Islington 12, Westminster 10), Northumberland 38 (Newbiggin by the Sea U.D. 18), Suffolk 31 (Blyth R.D. 31), Middlesex 24 (Ealing M.B. 11), and Leicestershire 23 (Leicester C.B. 19).

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in May was 102, compared with 116 in the previous month and 73 (revised figure) in May, 1954.

The number of cases of industrial diseases in the United Kingdom reported during May, 1955, was as follows: lead poisoning 1, aniline poisoning 3, mercurial poisoning 1, compressed air illness 1, anthrax 1, epitheliomatous ulceration 12, chrome ulceration 22; total 41. There was 1 death from epitheliomatous ulceration due to pitch and tar.—*Ministry of Labour Gazette*, June, 1955.

Medical News

King Edward's Hospital Fund for London.—During the last five years the King Edward's Hospital Fund has spent £136,000 on mental and mental deficiency hospitals. Now the Fund's intervention is to be greatly increased. At the annual meeting on June 27 at St. James's Palace, London, it was decided to allocate £250,000 for this purpose during the triennium 1955–7. The Metropolitan area, said the DUKE OF GLOUCESTER, who presided at the meeting, was served by some 36 large mental hospitals and mental deficiency institutions, and a survey had shown the outstanding needs to be modernization of their buildings and the provision of a hospital environment for the patients more in keeping with present-day attitudes to the mentally sick and the results of treatment. It was explained that the £250,000 would be spent as follows: £100,000 for general amenities, £50,000 to improve catering services, and £100,000 for three pioneer schemes in rehabilitation. These are an occupation centre at Goodmayes Hospital, Ilford, which would provide training in typing and office work, light metal work, carpentry, printing, and other trades; a social centre at Warlingham Park Hospital, built on the lines of a village centre with shops, hairdresser, bank, library, and a café so that patients could be helped in their return to normal social activities; and lastly a community centre and day hospital linked to the out-patient department of Bromley Hospital where patients would be given opportunities to live a wider social life. These three schemes, by ensuring thorough rehabilitation, aim at reducing the length of hospitalization of mental patients and the risk of relapse.

Drug Traffic in Britain.—Illicit traffic in drugs in the United Kingdom and Northern Ireland remains on a small scale, according to the Government's report to the United Nations for the year 1954. Opium traffic, confined largely to people of Chinese origin, is declining, and there is no knowledge of any illicit production of synthetic narcotics, those that find their way on to the market being diverted from lawful sources. However, seizures of Indian hemp showed a marked increase last year, 118 kg. being confiscated during 1954. The hemp is used almost exclusively by people of African, West Indian, or Asiatic origin. The number of known addicts in Britain, with an estimated population of about 50 millions, was 317. Of the 148 men 66 were doctors, but of the 169 women only 3. Morphine was used alone or in combination with other drugs by 65% of the known addicts, heroin by 17%, and pethidine by 16%. There were no exports of dangerous drugs to the few countries which have no import certificate system, and only two firms, both in Edinburgh, were licensed to manufacture heroin. No heroin was imported during the year, and none exported to the United States.

Drug Addiction in Canada.—In Canada, with a population at the 1951 census of 14 million, the number of drug addicts to-day is 3,212, according to an estimate in the recent report to the Senate of the Reid committee on the traffic in narcotic drugs. Half of the 2,364 "criminal addicts" are said to be in Vancouver, whose police department is criticized in the report for its laxity in tackling the problem. The Reid committee satisfied itself that there is no juvenile addiction problem in Canada, only 26 of the criminal addicts being under 20 years of age. Heroin is the drug most commonly used.

Prevention of Poliomyelitis.—Since our last note on the American poliomyelitis vaccine programme (June 18, p. 1485) there have been three major developments: (1) Workers from California University, in a report in *Science*, claim to have succeeded in culturing the three types of poliomyelitis virus in human amniotic membrane (*New York Times*, July 1). If this work is confirmed and the method proves applicable to commercial production, the need for monkeys, whose kidneys are used at the moment in making Salk vaccine, may be greatly reduced. (2) A conference of poliomyelitis workers, convened by the National Foundation for Infantile Paralysis on June 18 in New York, discussed whether the risk of vaccination causing local paralysis justified suspension of poliomyelitis inoculations during the summer season. "The slight hazard of provocation," said the conference in an agreed statement, "is insufficient to limit the injection of poliomyelitis vaccine even in the presence of a rising incidence of poliomyelitis in the community." (3) Another recommendation to continue vaccination during the summer was made in Washington on June 23 by a panel of scientists giving evidence before a subcommittee of the House of Representatives. However, their decision was not unanimous, the voting being eight to three in favour of continuation, with four abstentions. During the previous day's hearing both Dr. ALBERT SABIN and Professor JOHN F. ENDERS had expressed themselves in favour of replacing the virulent Mahoney strain in the Salk vaccine by a safer one (*New York Times*, June 23 and 24). This view was endorsed by the others on the panel.

Order of St. John.—Four Bailiffs Grand Cross of the Venerable Order of St. John have been gazetted this week. This is a very high honour, as apart from members of the Royal Family the number of Bailiffs Grand Cross is limited to ten. Three of the new Bailiffs are surgeons, Sir JAMES ELLIOTT, of New Zealand, Sir HUGH POATE, of Australia, and Lord WEBB-JOHNSON; the other is the Rt. Hon. VINCENT MASSEY, Governor-General of Canada. Sir James Elliott is a leading member of the medical profession in New Zealand. Until last year he was Chancellor of the New Zealand Priory of the Order. He is a member of the New Zealand Board of Health and Medical Research Council and honorary consulting surgeon to the Wellington Hospital. He is also a past president of the New Zealand Branch of the B.M.A. and a former editor of the *New Zealand Medical Journal*. New Zealand now has the distinction of being the first of the Priories outside Britain to have two Bailiffs Grand Cross, the other New Zealander to receive this honour being the Hon. Sir HEATON RHODES in 1947. Sir Hugh Poate is Chancellor of the Priory in Australia, a past president of the Royal Australasian College of Surgeons, and honorary surgeon to the Royal Prince Alfred Hospital, Sydney. Lord Webb-Johnson was until last year Hospitaller of the Grand Priory in the British Realm.

British Association of Paediatric Surgeons.—The annual meeting was held in Glasgow from June 15 to 17, and in the absence of the president, Mr. MATTHEW WHITE, on account of illness, the chair was taken by Mr. A. P. LAIRD. Seventy delegates and their wives attended, Europe being represented by paediatric surgeons from Denmark, Sweden, Holland, Finland, Germany, Portugal, and Greece; Mr. D. G. MCKAY and Mr. K. B. FRASER represented Australia. Papers were read each morning at the Royal Faculty of Physicians and Surgeons, the subjects including hydrocephalus, burns, pyogenic arthritis, chronic retention of urine, intussusception, perforation of the common bile duct in infants, enuresis, cleft lip and palate, and haemangioma. Clinical, pathological, and photographic demonstrations were held at the Royal Hospital for Sick Children. The PRINCIPAL OF THE UNIVERSITY OF GLASGOW received the delegates at a sherry party in the College Rooms, and there were tours around the Trossachs, Loch Katrine, and Ayrshire. The meeting concluded with a dinner at the Royal Faculty of Physicians and Surgeons.

Clinical Research Fellowships.—The Medical Research Council has made the following new appointments to Fellowships in clinical research for the academic year 1955–6: Dr. D. A. DAVEY (medical research fellow, St. Mary's Hospital, London), Dr. A. H. GOWENLOCK (resident clinical pathologist, Manchester Royal Infirmary), and Dr. S. H. TAYLOR (senior house officer, Department of Medicine, Queen Elizabeth Hospital, Birmingham).

National Spastics Society.—The annual meeting of the National Spastics Society, a lay association for the welfare of patients with cerebral palsy, was held at London County Hall on July 2, and was attended by representatives of the more than 100 local groups of the Society in various

parts of the kingdom. Mr. DAWSON SHEPHERD, chairman of the executive committee, described the Society's plans for raising £350,000 this year for the maintenance of special schools (two more of which had been opened during the past year) and treatment centres, and the establishment of new ones. Last year nearly £400,000 had been raised. Medical research was also an important part of the society's programme under a medical director, and the planning of such research was well under way. They were encouraged by the fact that the Medical Research Council was undertaking research into cerebral palsy and that hospital boards were increasingly interested in the subject. The attitude of the local authorities towards any project on behalf of handicapped children was invariably sympathetic. The biggest problem and challenge, said Mr. Shepherd, was the employment of spastics, and no one, apparently, could tell them how to solve it. No doubt a large number of adult spastics were unemployable, but he felt that more could be done, given a businesslike and energetic outlook.

Society for the Relief of Widows and Orphans of Medical Men.—At the annual meeting on June 15 in London, with the president, Sir ROBERT YOUNG, in the chair, the treasurer, Sir ERNEST ROCK CARLING, reported that the value of the society's investments at the end of last year was £146,000. During the year a total of £4,352 had been distributed to 32 necessitous doctors' widows in the form of grants and presents. Doctors interested in joining the society may obtain information from the secretary at 11, Chandos Street, Cavendish Square, London, W.1.

Professor Winifred Cullis, emeritus professor of physiology of London University and for many years professor of physiology at the London School of Medicine, received the honorary LL.D. of Birmingham University on July 2. It was at Birmingham that she spent her childhood and schooldays. One month earlier, on June 2, Professor Cullis celebrated her eightieth birthday, and all her friends will wish to congratulate her. Besides her academic distinctions, Professor Cullis has many outside interests: she is a past-president of the International Federation of University Women and deputy-chairman of the English-Speaking Union. During the war she was head of the women's section of the British Information Services in the United States (1941–3), and later she toured the Middle and Far East, at the Government's request, to describe the part British women were playing in the war.

Mr. L. R. Broster, surgeon to Charing Cross Hospital and chairman of the committee of management of the Empire Medical Advisory Bureau of the British Medical Association, was the recipient during the Joint Annual Meeting in Toronto of the Bronze Medal of the South African Medical Association. In making the presentation, Dr. A. H. TONKIN, medical secretary of the South African Medical Association, spoke of the links of Commonwealth solidarity which Mr. Broster had helped to forge.

Dr. J. A. Fraser Roberts, lecturer in medical genetics at the London School of Hygiene and Tropical Medicine and the Institute of Child Health (London University), has been elected a vice-president of the Royal Anthropological Institute.

Dr. J. C. Gregory, who is in general practice at Hemel Hempstead, has been elected chairman of the All England Lawn Tennis Club. From 1926–30 he represented Great Britain in the Davis Cup. In 1929 Dr. Gregory was ranked as England's No. 1 player (with H. W. Austin), and he was the first Englishman to be seeded at Wimbledon. In that year, also, he won both the Australian and Scottish championships.

COMING EVENTS

Symposium Neuroradiologicum.—This meeting, designed particularly for radiologists, neurologists, and neurosurgeons, will be held in London from September 13–17. Further information from the secretary, Dr. R. D. HOARE, National Hospital for Nervous Diseases, Queen Square, London, W.C.1.

University of St. Andrews.—The Medical Faculty will hold a symposium on the pulmonary circulation and respiratory function on September 15 and 16. Details from the Convener of Postgraduate Medical Studies, Queen's College, Dundee.

NEW ISSUES

Thorax.—The new issue (Vol. 10, No. 2) is now available. The contents include:

THE CLINICAL SIGNIFICANCE OF POSITIVE CULTURES AND OF ISONIAZID-RESISTANT TUBERCLE BACILLI DURING THE TREATMENT OF PULMONARY TUBERCULOSIS. Wallace Fox and Ian Sutherland.
CONGENITAL TUBERCULOSIS. Beryl D. Corner and N. J. Brown.
STRANGULATED DIAPHRAGMATIC HERNIA IN THE NEONATAL PERIOD. P. P. Rickham.
THE HISTOLOGY OF LUNG CANCER. J. B. Walter and D. M. Pryce.
THE SITE OF ORIGIN OF LUNG CANCER AND ITS RELATION TO HISTOLOGICAL TYPE. J. B. Walter and D. M. Pryce.
RESPIRATORY FUNCTION FOLLOWING PULMONARY INFARCTS. Ove Jacoby, Tyge Søndergaard, and H. H. Wandall.
MALIGNANT CHANGE IN BRONCHIECTASIS. R. J. R. Cureton and I. M. Hill.
THE LATE RESULTS OF THE CONSERVATION OF THE APICAL SEGMENT OF THE LOWER LOBE IN RESECTIONS FOR BRONCHIECTASIS. E. Hoffman.
INTRALOBAR SEQUESTRATION OF THE LUNG. R. Abbey Smith.
FACTORS LEADING TO THE DEVELOPMENT OF A JOINT BETWEEN THE MANUBRIUM AND THE MESOSTERNUM. G. T. Ashley.
FOREIGN BODY GRANULOMATA OF THE LUNGS DUE TO LIQUID PARAFFIN. J. C. Wagner, D. I. Adler, and D. N. Fuller.
CAUSTIC STRICTURES OF THE OESOPHAGUS. Paul Marchand.
NORADRENALINE AS A VASOCONSTRICTOR IN LOCAL ANAESTHESIA FOR THORACOPLASTY. H. E. Bell.

Issued quarterly; annual subscription £2 2s; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, July 9

FACULTY OF ANAESTHETISTS: ROYAL COLLEGE OF SURGEONS OF ENGLAND.—10.30 a.m., scientific meeting. Speakers, Lord Adrian, Dr. W. Grey Walter, Dr. B. D. Wyke, and Mr. W. Blackwood. Details from the secretary of the Faculty.

Tuesday, July 12

INSTITUTE OF NEUROLOGY.—5 p.m., Professor G. Fanconi (Zurich): Pathomorphosis of Some Diseases of the Central Nervous System Occurring in the Last Fifty Years.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., F. E. Williams Lecture by Lord Amulree: Modern Hospital Treatment and the Pensioner.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Moynihan Lecture by Professor H. Olivecrona (Stockholm): Hypophysectomy.

Wednesday, July 13

ASSOCIATION OF CLINICAL BIOCHEMISTS.—At Meyerstein Lecture Theatre, Westminster Medical School, 5.30 p.m., Dr. Donald D. Van Slyke: Outlines of an Interesting Case of Renal Disease.
ROYAL SANITARY INSTITUTE.—6 p.m., Dr. J. D. Kershaw: Public Health Nurse of the Future.

Thursday, July 14

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—6 p.m., Dr. Evelyn Robe (Chicago): Cinematograph film demonstrating the Physiology of the Larynx.

Friday, July 15

BIOCHEMICAL SOCIETY.—At Department of Agricultural Chemistry, University College of North Wales, Bangor, 11 a.m., 342nd meeting. Scientific papers.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Charles Tomes Lecture by Professor A. B. MacGregor: Treatment of Fractures of the Mandibular Condyle.

Saturday, July 16

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—10.30 a.m., symposium: Gastroenterology.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Grant.—On June 29, 1955, at Simpson Memorial Maternity Pavilion, Edinburgh, to Barbara Patricia, wife of Dr. P. W. Grant, 127, Mayfield Road, Edinburgh, a son—Iain Lorraine.
Roy.—On June 4, 1955, at Chiswick Maternity Hospital, London, W., to Bokul, wife of Dr. P. K. Roy, of Jatindramohon Avenue, Calcutta, a son.

DEATHS

Darling.—On June 8, 1955, at Kingston, Ontario, Canada, Janet Stella Darling, M.B., Ch.B., of Edinburgh, aged 29.
Doubble.—On May 16, 1955, at St. Richard's Hospital, Chichester, Sussex, Meredith Sedgwick Doubble, M.R.C.S., L.R.C.P., formerly of Somersham, Hunts.
Jones.—On May 18, 1955, at 92, Maison Dieu Road, Dover, Kent, Arthur Edward Booth Jones, M.D., Lieutenant-Colonel, R.A.M.C., retired, aged 76.
Kidston.—On May 13, 1955, at 25, Western Parade, Southsea, Hants, Noel Wallace Kidston, M.B., Ch.B., aged 73.
McLatchie.—On May 20, 1955, in hospital, John Drummond Pryde McLatchie, M.D., of Upper Wimpole Street, London, W., and 27, Sandy Lodge Road, Moor Park, Rickmansworth, Herts, aged 84.
Selby.—On May 6, 1955, at Newton House, West Bowling, Bradford, Yorks, Edward Arthur Selby, M.R.C.S., L.R.C.P.
Sproule.—On May 15, 1955, in hospital, James Chambers Sproule, C.B.E., L.R.C.P.&S.I. & L.M., D.P.H., Brigadier, late R.A.M.C., retired, of Old Bell House, Somerton, Somerset, aged 67.

Any Questions ?

Non-virulent Diphtheria Bacillus

Q.—*A heavy growth of C. diphtheriae (gravis type) was isolated from a boy, immunized against diphtheria in infancy, who had a sore throat and cervical adenitis. He made a rapid recovery in two or three days with antitoxin, but he continues to carry the organism two weeks after the onset of the illness. Bacterial examination shows that the organism does not produce toxin. (1) Should this patient be regarded as a true case of diphtheria? (2) Is his organism dangerous to others? (3) Is any treatment required to deal with the carrier state?*

A.—For practical clinical purposes an organism which does not produce toxin is non-virulent. A very small percentage, about 1% to 5%, of gravis type of *C. diphtheriae* are non-virulent. This patient should not be regarded as a true case of diphtheria, his organism is not dangerous to others, and no treatment is required to deal with the carrier state. His sore throat and cervical adenitis were almost certainly due to another organism, probably a haemolytic streptococcus, and the presence of this non-virulent *C. diphtheriae* is of no clinical or epidemiological significance.

Management of Puerperal Mastitis

Q.—*(a) What is the treatment of puerperal mastitis in the early stages of flushing and hardening? (b) If an abscess has formed, should antibiotics be used? Should the breast be expressed or left alone and poulticed? Should the expressed milk be given to the baby? (c) How may breast abscesses be prevented?*

A.—Puerperal mastitis is best treated when there is no more than a slight flush and tenderness over one area of the breast, this having been brought to notice by the patient suddenly experiencing a chill and malaise. At this time crystalline penicillin, one million units, followed by half a million units 12-hourly, usually restores the breast to normal within 36 hours. At a later stage, when reddening is accompanied by induration, such treatment continued for four or five days may still be effective, but once there are signs that an abscess has formed immediate incision and drainage takes precedence. In this respect it should be noted that antibiotics sometimes modify the clinical picture of breast abscess, so that pus may be present without pyrexia and without typical local signs. In such a case oedema of the skin of the breast is one of the most reliable signs. Aspiration of the abscess is sometimes advised as an alternative to incision, but the results are unsatisfactory. Surgery may be supplemented with antibiotic therapy, the nature of the antibiotic being governed by the bacteriological examination of the pus.

Mastitis at any stage calls for immediate cessation of suckling from the affected breast, and even if milk is removed by other means it should *not* be given to the baby, for it is likely to contain pathogenic organisms. Engorgement of the breast is detrimental to its quick recovery from infection, but removal of milk by expression or by pump can be even more harmful. Stilboestrol, 5 to 10 mg. four-hourly, should therefore be given early in an attempt to prevent or control engorgement, but local measures should be avoided as far as possible. The breast should be kept comfortably supported, but poulticing probably does more harm than good.

In the case of a flushed breast, suckling on the sound side is usually continued, and it can be resumed on the affected side within two or three days if the mastitis clears quickly. In the case of abscess formation, however, it is usually best to discontinue breast-feeding completely.

Epidemic mastitis, the infection affecting the ducts and glands, can occur in institutions. Its prevention depends on the elimination of sources of infection and of cross-infection. The common type of mastitis, however, begins as a cellulitis, the organisms probably gaining entrance through an injury (often a very small abrasion) to the nipple. Lowered tissue-resistance resulting from engorgement, associated with puerperal bacteraemia, is another possibility. In either case prevention of mastitis depends on the preparation and care of the nipples during pregnancy and the puerperium, on the prompt and careful treatment of engorgement, on the technique of breast-feeding, and on the woman's standard of hygiene—matters which occupy at least a chapter in standard textbooks. It may be added that abscess formation can usually be prevented by *early* diagnosis and prompt and adequate treatment of mastitis.

Vaccine Therapy in Disseminated Sclerosis

Q.—*Is there any convincing evidence that vaccines are useful in the treatment of disseminated sclerosis? If so, how do they act?*

A.—The prolonged and remittent course of disseminated sclerosis makes the evaluation of any mode of treatment difficult. It is generally agreed that the necessary criteria are: (1) the effect on acute symptoms; (2) the prevention of relapses; and (3) the effect on disability.[1] Follow-up for a period of some five years is required.

The writer has no knowledge of any report on the use of vaccines which satisfies these criteria. Four consecutive relapses in a single patient following within 60 hours of weekly injections of an autogenous vaccine have been described.[1]

REFERENCE

[1] McAlpine, D., Compston, N. D., and Lumsden, C. E. (1955). *Multiple Sclerosis*. Livingstone, Edinburgh and London.

Treatment of Tension

Q.—*I have a patient, a flying officer, who finds it very hard to relax. He is of the anxious, obsessive, highly conscientious type, and, owing to his flying duties, cannot take sedatives such as phenobarbitone. What treatment is advised? Would exercises in relaxation help, and, if so, could you please give practical details?*

A.—It is assumed that the patient has a chronic tension state in which depressive features are absent or transient and slight. In such a case, since sedatives are excluded, treatment may consist of psychotherapy, relaxation therapy, or both. The existence of a formulated personality problem—for example, a sexual one—or difficulties in maintaining satisfactory relationships with other people, would indicate the need for psychotherapy. An anxious and obsessional patient such as is described would not benefit from psychoanalysis, and psychotherapy should be conducted on a fairly superficial level and should be directed towards the manipulation of habits and attitudes so that tension is less easily generated.

Relaxation treatment could very well be tried first, and in a number of instances is successful by itself. Supervision during the first six or nine sessions is required, and this should be undertaken by a doctor or a physiotherapist accustomed to the technique as employed with psychiatric patients. The method is first taught in recumbency, and attention is successively directed to the hands, arms, face, and neck. The objective is to place the voluntary musculature in such a position that centripetal proprioceptive impulses are abolished. By practice twice a day for 15 minutes each time, supported by a teaching session once or twice a week, the average patient of the kind described will learn the technique quite satisfactorily. Once he has been convinced of its rational basis he may well turn on to the method all the drive of his obsessional character. He then goes on to practise attenuated relaxation in the sitting position, and by a process of physiological "facilitation" learns to keep his tension at bay during the ordinary events of everyday living. A more complete account of the method as applied to this type of patient may be found in *Muscle Relaxation* by Dr. G. Garmany, published by the Actinic Press, London, 1952.

Sexual Intercourse after Coronary Thrombosis

Q.—*A patient of 54 has recently had a moderately severe coronary thrombosis. What advice should I give him concerning sexual intercourse?*

A.—This problem should be managed as other problems involving moderate muscular activity. If the infarct has been small and recovery good there is no need to make any significant change of habit. Patients may need reassurance that no harm is likely to result. If the effort brings on pain or breathlessness the patient will usually find his own way of reducing exertion. Digitalization or a tablet of nitroglycerin before the act may help. The problem usually solves itself in other ways. Illness and the inevitable accompanying anxiety tend to diminish libido. Even the enthusiastic polygamists of the Old Testament recognized the arrival of a time "when desire shall fail."

Digitalis and the Easy Labour of Cardiac Patients

Q.—*Has digitalis any known action on the uterus that might explain why cardiac patients tend to have easy labours? If so, would digitalis be of any value in uterine inertia?*

A.—Digitalis has no known action on the smooth muscle of the uterus. Experimentally, however, there is a demonstrable action on skeletal muscle (e.g., rat diaphragm), when this has become fatigued.

The fact that cardiac patients have relatively easy labours is a complex affair which may be related to a tendency to premature delivery. The cardiac patient is often capable of short bursts of physical exertion so long as there is an adequate interval to allow recuperation. For this reason the strain of a normal delivery in a patient with heart disease is often less than might be imagined. There is certainly no evidence that digitalis is of any special value in uterine inertia.

Second Doses of Serum

Q.—*Is it true that the therapeutic effect of an antitoxic serum is largely neutralized if a patient has previously had either the same serum or any other injection containing horse serum. If so, what is the mechanism of this effect and for how long does it persist?*

A.—It is truer to say that the therapeutic effect of an antitoxic serum *may be* largely neutralized if a patient has received a previous dose of any kind of serum of horse origin.

Horse serum, whether crude or concentrated in some way, is a foreign protein to human subjects and may therefore incite the production of an antibody, anti-horse precipitin. There is probably great individual variation in the ease with which different persons produce precipitins. If, however, this antibody is present in the blood stream when a second dose of antitoxic serum is given, this dose may be neutralized and rapidly eliminated. There is some evidence that precipitins may persist in a patient's circulation for at least six months after a dose of 1,500 units of tetanus antitoxin.

If an interval of several years elapses between a first and a second dose of antitoxin, circulating precipitins may be absent. The patient may, however, be sensitized to horse protein, and produce precipitins within a very few days of the second dose of serum. The beneficial action of this second dose of antitoxic serum would, in such a case, be very short-lived. There is therefore a very strong case for general active immunization against diphtheria and tetanus. Doses of tetanus antitoxin are given increasingly, and there is always the danger that a patient who has received an earlier dose of serum of some kind may derive no benefit from a second injection. How frequently this may occur is a matter for speculation. The questioner might be interested in a case report on such an occurrence.[1]

REFERENCE

[1] *British Medical Journal*, 1954, **2**, 444.

Free Milk in Industry

Q.—*I attend as factory doctor a large light-engineering works. It has been the custom from time immemorial for all painters, sprayers, and those working on machines giving off cast iron dust to receive a daily milk ration supplied by the firm. The men take their milk more seriously than anything else, feeling that without it they would succumb to some fatal disease. The practice is spreading, and costing the firm hundreds of pounds a year. Is there any basis for the belief that the milk is necessary?*

A.—Though milk drinking has been traditional in certain lead trades for many years the extension of the habit to other processes and factories is of more recent origin, having started in the 1930s. The virtue of the practice in those days lay in the additional first-class protein provided for men, many of whom were on "short time." When milk was in short supply during the war and canteen meals were widely available most firms dropped the additional milk except for those on a few special processes.

There is *no* basis for the belief that milk is necessary for "all painters, sprayers, and those working on machines giving off cast iron dust." There is perhaps a little evidence that milk is of value in those exposed to a *heavy* lead hazard, but lead hazards of this magnitude are very few to-day and should certainly not exist outside the special lead processes requiring statutory routine medical inspection. With this very small exception there is no reason whatsoever for milk to be provided in industry as a vague prophylactic against all dust and fume; it has no such properties. If milk is to be provided free by employers it should be to those who need it, and these may be found among the ranks of young persons and those who suffer from peptic ulcer.

Yellow Fever Vaccination

Q.—*May I ask the following questions, prompted by recent reports of encephalitis in infants following yellow fever vaccination? First, what is the dose of yellow fever vaccine for infants? Secondly, is it necessary to inoculate against yellow fever travellers coming from an endemic to a non-endemic country, such as Britain?*

A.—Infants are given a full dose, usually in a volume of 0.5 ml. of chick-embryo vaccine (17 D). When infants under the age of 9 months are to be vaccinated against both yellow fever and smallpox, it is now recommended that there should be an interval of 21 days between the two vaccinations, no matter which is performed first.[1]

So far as Britain is concerned, the answer to the second question is "no." But some non-endemic countries have been declared as "yellow fever receptive areas," and demand the yellow fever immunization within six years of all travellers who have passed through or have left a yellow fever zone. Information about requirements is obtainable from embassies or consulates or from the medical or traffic departments of the transport companies concerned.

REFERENCE

[1] *Monthly Bull. Minist. Hlth (Lond.)*, 1955, **14**, 95.

Permanence of Signs of Sodomy

Q.—*If it takes, as I think, three or four full penetrations to establish positive signs in the anus of a passive partner in sodomy—i.e., absence of perianal puckering, loss of sphincter tone, funnel shape on separating the nates, and, perhaps scars—would these signs disappear if there were no more acts of sodomy?*

A.—Your inquirer is not correct in his assumption. One forcible penetration may cause the production of small mucosal tears or fissures, or if the opening is small and inelastic even more serious injury. Loss of perianal puckering and sphincter tone are usually the result of many acts, and the funnel appearance is also the result of long practice. In my experience, once these signs are present, the opening never returns to its normal appearance completely.

Morphine in Patients with Raised Intracranial Pressure

Q.—*In a person with increased intracranial tension due to a cerebral tumour, is it dangerous to give morphine to alleviate the severe headache?*

A.—It is established that in the presence of raised intracranial pressure not only may slowing and irregularity of respiration occur, but also respiratory arrest. These disturbances are due to impairment of the blood supply of the respiratory centres in the brain stem and are often evidence of a foraminal or tentorial pressure cone. It is likewise well established that morphine depresses the respiratory centre, and it is clear that the combined action of pressure and morphine could be highly dangerous. Of course, if investigation has established the malignancy and inoperability of a patient's cerebral tumour, all that remains is to relieve symptoms, and morphine would then be justifiable, in spite of its risks, if posture, magnesium sulphate enemata, and analgesics which do not produce respiratory depression were of no avail.

Dermographism

Q.—*I have a patient who suffers from dermographism. He develops weals from very slight stimuli, and finds these very embarrassing when swimming, etc. I have suggested to him that he might try the effect of antihistamines, but I wondered if there was any way of altering the sensitivity of the skin.*

A.—Intensive investigations into possible physical causes of dermographism have usually yielded no useful results, but occasionally psychiatric factors are blamed. In most cases the disorder starts abruptly, lasts for a period of some months or years, and then eventually clears up. It is very doubtful whether any treatment is truly curative, but the antihistamine drugs will nearly always produce some symptomatic improvement. It may be a good plan to try several of these substances, with different dosage, so as to determine which suits the individual patient best and with the minimum side-effects. Once this has been decided there is no objection to continuing suppressive treatment until the disorder clears up.

Books on Sex

Q.—*Could your expert please recommend one or two sound books on sex instruction for each of the three following groups: (a) adolescents, (b) engaged couples, (c) married people in difficulties?*

A.—(*a*) *Adolescents:* For girls: *Attaining Womanhood.* For boys: *Attaining Manhood.* These are companion volumes, in part identical, both written by George W. Corner and published by George Allen and Unwin, Ltd., London.

(*b*) *Engaged Couples:* (1) *The Art of Marriage,* by Mary Macauley, Delisle, Ltd., London. (2) *The Sex Factor in Marriage,* by Helena Wright, Williams and Norgate, Ltd., London. (3) *Your Marriage,* by Kenneth Walker, Secker and Warburg, London.

(*c*) *Married People with Difficulties:* (1) *Any Wife or Any Husband,* by Medica (Dr. Joan Graham), Wm. Heinemann Medical Books, Ltd., London. (2) *Ideal Marriage,* by Van der Velde, Wm. Heinemann Medical Books, Ltd., London. This book enters into great detail about the technique of physical love and, while helpful to many, might have a deterrent effect on certain sensitive individuals.

Spectacles in the Theatre and in Ophthalmoscopy

Q.—*I wear spectacles. Could you please let me know (a) the best way of preventing them "steaming up" during a long operation, and (b) the best way of using an ophthalmoscope when wearing them?*

A.—(*a*) "Steaming up" of ordinary spectacles during a long operation is mainly the result of wearing a face-mask. This condensation of the cooped-up expired air can usually be avoided if the operator wears semilunar spectacles in the theatre. As the upper half is missing in each glass, ventilation tends to prevent the vapour from condensing. If this device should fail, then the spectacles can be covered with a thin film of anti-vapour substance, which most dispensing opticians store.

(*b*) There is no special trick about ophthalmoscopy by a spectacle-wearer. Most people prefer to remove their glasses while using the ophthalmoscope, and, if their refractive error is considerable, they rotate the appropriate lens into the ophthalmoscope's sight-hole. Others habitually look through their own glasses when they use this instrument. It is a matter for individual taste.

Chemoprophylaxis against Filariasis

Q.—*Is chemoprophylaxis against filariasis (W. bancrofti) practicable, either as a short-term measure during times of heavy exposure or for longer periods?*

A.—No simple method of chemoprophylaxis against filariasis due to *W. bancrofti* is known at present, but it is doubtful whether such a procedure would be worth while even if it were available. To produce pathological lesions, such as elephantiasis or lymphangitis in Africans, years of exposure to large numbers of infected mosquitoes are necessary; and even then only a small proportion of the persons successfully invaded by the worms actually show lesions. Although bancroftian filariasis sometimes occurs among Europeans in the Pacific Islands, it is practically unknown among Europeans in other parts of the Tropics who take the ordinary precautions against mosquitoes.

Experimentally there are a few indications as to how chemoprophylaxis might be attempted. Large doses of diethylcarbamazine ("hetrazan," "banocide") seem to have a weak protective action in cotton rats exposed to intense infection by the filarial parasite *Litomosoides.*[1] During a short period of heavy exposure it would be possible for a person to take carbamazine, 200 mg. thrice daily, but the writer would not dream of doing so himself as a protective measure. Alternatively, Kershaw and Williamson[2] have shown that a single intramuscular injection of an antimony compound called MSb protected cotton rats for six months against infection by *Litomosoides.* This compound, which is not commercially available, forms a deposit at the site of injection from which it is slowly absorbed. It has never been tried for this purpose in man, but scientists would be interested to learn of its experimental use and of its effects.

REFERENCES

1 Hawkings, F., Sewell, P., and Thurston, J. P., *Brit. J. Pharmacol.*, 1950, **5**, 217.
2 *Ann. trop. Med. Parasit.*, 1952, **46**, 268, 320.

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